

Author Index

(Italicized page numbers refer to comments in General Discussions)

Abrams, W. B., 98
Apostolides, A., 254-266

Blackburn, H., 36, 58, 66, 236-242
Blaufox, M. D., 254-266
Blumenthal, S., 28-32, 36-37
Borhani, N. O., 254-266

Cooper, R., 110, 388
Curran, J. P., 320-330
Curry, C. L., 363-372
Cutter, G., 254-266

Dustan, H. P., 460-462
Daugherty, S., 254-266

Ferguson, D. C. E., 222-235
Fitz, A. E., 267-288
Fodor, G., 200
Frohlich, E. D., 58, 68-73, 109-110, 125, 267-288

Gibson, E. S., 390-403
Goldman, A. I., 267-288

Haber, P., 463-465
Hammond, J. J., 147-160
Hawthorne, E. W., 292, 363-372
Haynes, R. B., 390-403
Hunt, J. C., 373-380, 389

Johansen, H. L., 203-219
Johnson, A. L., 390-403
Julius, S., 38-52, 58

Kannel, W. B., 16-17, 58, 128-139, 144-146, 161-164
Kass, E. H., 36, 110, 201, 253, 291, 318-319, 412-419, 423
Kilcoyne, M. M., 33-35, 36
Kirkendall, W. M., 146, 147-160, 176, 200-201, 359, 361

Klimt, C. R., 250-252, 253, 289
Krug, S., 411

Labarthe, D. R., 3-14, 16-17, 37, 58, 422-423
Langford, H. G., 16, 98, 145, 175, 198-199, 200, 289-290
Laragh, J. H., 165-174, 175-177
Lavin, M. A., 267-288
Levy, R. I., 441-457
Lewin, A. J., 254-266

Marston, M.-V., 404-409
Melmon, K. L., 112-122, 125-127
Meneely, G. R., 201, 361
Miall, W. E., 18-25, 422-423, 458-459
Miller, M., 98, 253, 318
Moser, M., 16, 126, 331-332, 360, 388, 410-411
Moses, C., 84-95, 410-411

Neri, L. C., 203-219

Ostfeld, A., 107-108, 109-110
Overturf, M. L., 147-160

Page, L. B., 25, 83, 175, 200, 290-291, 361-362
Paul, O., 59-63, 66
Perry, H. M., Jr., 1-2, 220-221, 267-288, 290-292, 472-475
Petursson, S. R., 320-330
Pickering, G., 27, 289-290, 439, 466-471
Polk, B. F., 254-266, 290

Ramirez, E. A., 81-82, 98, 110-111
Reader, R., 15, 67, 146, 309-317
Redmond, D. P., 222-235
Remington, R. D., 244-249
Richman, H. G., 267-288
Roberts, R. S., 390-403,
Robertson, J. I. S., 64-65, 66, 126, 144, 176-177

- Sackett, D. L., 390-403
 Saunders, E., 37, 96-97
 Schwartz, G. E., 222-235
 Schnall, P., 109, 360, 439-440
 Schnaper, H. W., 267-288, 381-385, 388
 Schoenberger, J. A., 420-421
 Schork, M. A., 38-52
 Shapiro, A., 98, 109-110, 123-124, 126, 175-176, 222-235, 318
 Sheiner, L. B., 112-122
 Slotkoff, L. M., 200
 Smith, W. M., 74-80, 83, 291-292, 293-308, 319, 472-475
 Sondik, E. J., 441-457
 Stamler, J., 140-143, 144-146, 201-202, 263, 318-319, 333-358, 360-361
 Stamler, R., 410, 439
 Stason, W. B., 424-436, 439-440
 Steele, B., 267-288
 Strasser, T., 243, 291, 319, 440
 Syme, S. L., 99-106, 109, 111
 Tarazi, R. C., 53-57
 Taylor, D. W., 390-403, 410-411
 Thomsen, G. E., 363-372
 Thurm, R. H., 201
 Tobian, L., 178-197, 200-201, 410
 Tuckman, J., 66, 253, 423
 Ward, G. W., 437-438
 Wardell, W. M., 320-330
 Weinstein, M. C., 424-436
 Weiss, S. M., 222-235
 Wilber, J., 16, 109, 386-387, 388, 440

Subject Index

- A**
Adrenal disorders, 365
 Adrenal hormone levels, 161
 Adrenergic-neurone blocking drugs, 326-328
Age factors, 4, 12, 58
 in antihypertensive therapy, 70-72
 complications of hypertension and, 59
 in interventions, 11
 low-renin hypertension and, 162
Albany Civil Servant Study, 140
Aldosterone
 in malignant hypertension, 162
 in primary hypertension, 161
 salt taste threshold and, 200
American Heart Association, Committee on Ethics of, 418
Angina pectoris, 78
Angiotensin, 161
Animal protein, 201-202
Antihypertensive drugs, 89-90
 benefit-risk ratios in, 355
 for children, 31-32
 in clinical trials, 313, 315
 consumption patterns of, 320-329
 evaluation of, 225
 holistic treatment and, 145
 in mass treatment, 346-347
 for mild hypertension, 68-72
 side effects of, 283-286
 adverse, 84-98
 patient compliance and, 100-101, 410-411
 placebo effect and, 107
 in Stepped-Care Program, 296
 utility function of, 112-127
 See also specific drugs
Arterial endothelium, changes in, 148
Arterial pressure, 34
Arterial wall metabolism, 148
Aspirin Myocardial Infarction Study (AMIS), 444, 450
Association of American Medical Colleges, 251
Asymptomatic hypertension, 376
Atherosclerosis, 128-139, 145-147
 antihypertensive treatment and, 359
 blood pressure and, 128-129
 role of vasoactive agents in, 147-148
 in PHS hospital trials, 78, 79
Autoregulation of blood flow, 182-183
- B**
Baroreceptor reflex activity, 33
Behavioral modification, 224-232, 331
Behavioral problems, 99-101
Beta-adrenergic blocking agents, 64, 66
 national consumption patterns of, 322-323, 327
Biofeedback, 225-227, 230-231
Blacks
 antihypertensive therapy for, 70, 71
 blood pressure in, 33
 plasma renin activity in, 151-154
 See also Race factors
Blood lipids, 128-139
Blood pressure, 3-10, 164, 333-336
 body weight and, 239-240
 borderline elevations of, 135
 in children, 36-37
 lability of, 29
 measurement of, 34
 control of
 by biofeedback, 225-227
 complication rates and, 81
 educational program for, 68-69
 nonpharmacologic, 340-346
 by relaxation therapies, 228-229
 as coronary risk factor, 152, 293, 297-299
 effect of exercise on, 224, 237-238
 endocrine or renal problems and, 374-375
 genetic factors and, 19-24
 labile elevations of, 135
 mechanisms in regulation of, 161
 in prediction of hypertension, 41-42
 race and, 33, 257-259
 regulation by kidneys of, 161
 risk of coronary heart disease and, 135
 self-monitoring of, 400
 sodium intake and, 223
 effect of salt loading, 191-194
 stress and, 224, 231
 variability of, 467-469
 See also Diastolic pressure; Systolic pressure
Blood pressure reference curves, 37
Borderline hypertension, 7
 neurogenic, 45-46
 non-neurogenic, 46
 pathophysiology of, 44-46, 53
 predictors of, 58

- Borderline hypertension
 progression to moderate or severe hypertension from, 59-60
- Bronchitis, 203
- Bulbar input, 33
- C**admium, 204, 208-209, 220-221
- Calcium, 200
 in water supply, 204, 206-208
- Cardiac examination, 366
- Cardiac output, response to salt loading of, 191-194
- Cardiovascular system
 disease of
 magnesium and, 211
 mortality rate from, 79
 risk profile in, 133-134
 water hardness and, 203, 220-221
 neural control of, 33-34
- Casual blood pressure elevations, 16-17
- Central resetting of arterial pressure, 34
- Cerebrovascular complications, 60-61
- Chicago Heart Association Industry Study, 140
- Children
 detection and control of hypertension and hyperlipidemia in, 137-138
 precursors of adult hypertension in, 28-37
- Chlorthalidone, 291-292
- Cholesterol, 130-134, 140, 142
- Cigarette smoking, 259, 262, 347-348
 as risk factor, 138-143, 152, 293, 297-298
- Clinical trials, 318-319
 analysis and dissemination of results of, 454-457
 costs of, 418, 423, 450, 458-459
 design and management of, 244-253
 end points in, 423, 461
 ethical considerations in, 412-419, 451
 financing of, 250, 253
 planning of, 441-459
 treatment benefits measured in, 439
 worldwide, summary of, 309-316
 See also specific studies
- Clonidine hydrochloride, 92, 94, 96, 163
- Cold pressor test, 40
- Community high blood pressure treatment centers, 386-387
- Community health workers, 103-104, 109
- Compliance, *see* Patient compliance
- Complication rates, 81
- Comprehensive care, 347-348
- Congenital malformations, 203
- Cooperative trials, *see* Clinical trials
- Coronary Artery Surgery Trial (CAST), 442, 444
- Coronary Drug Project (CDP), 443
- Coronary heart disease, 78, 79
 as complication of hypertension, 60
 mild, 64
 hypertension, blood lipids and cigarette smoking as co-risk factors in, 128-139
 prevention of, 293
 risk factors in, 149-156, 293, 297-299
- Coronary Primary Prevention Trial (CPPT), 443-444, 447, 450, 454
- Cost-effectiveness, 426-432
 individual patient and, 440
 of nonpharmacologic treatment, 437-438
 of screening, 432-434
- Costs
 of clinical trials, 418, 423, 450, 458-459
 of treatment, 417-418
 direct, 425
 manpower impact, 425-426
 savings in cardiovascular treatment costs, 426
- Counseling, 31
- Cushing's syndrome, 365, 367
- D**ata management, 276-277
- Decision theory, 112-115
- Defense reflex, 289-290
- Diagnosis
 of hypertension in children and adolescents, 34
 of mild hypertension, 363-370, 373-380
- Diastolic blood pressure
 as risk factor, 293, 297-299
 pharmacologic treatment and, 334, 336
- Diet, 109, 110, 223, 348, 350-351
 low salt, 178, 331
 magnesium in, 213-215
 potassium in, 361
 rice-fruit, 201
 See also Obesity
- Diet-Heart Study, 319
- Diuretics, 183
 national consumption patterns of, 322-323, 326-327
- Doctor-patient relationships, 337-340, 352, 375-376
- Double Masters test, 78
- Drug therapy, *see* Antihypertensive drugs
- E**ating habits, *see* Diet
- Electrocardiogram abnormalities, 78, 152

- End points in clinical trials, 313, 461
 Environmental modification, 224
 Epidemiology, 47, 140
 salt intake and, 178-179, 207-208
 socioeconomic conditions and, 360
 water hardness and, 208-210
 Essential hypertension, 194
 nutritional therapy for, 378-379
 volume-dependent hypertension and, 163
 Ethical considerations
 in clinical trials, 412-423, 451
 in patient compliance, 390
 Exercise, 223-224, 237-238
 in mass treatment, 345
 in prevention, 241
 Extracellular fluid volume, 180-185
 regulation of blood pressure and, 161
 salt intake and, 193, 194, 201
 European International Working Group on Drug Utilization, 321
 European Working Party on Hypertension in the Elderly (EWPHE), 310, 311, 315
- F**
 Familial aggregation, 30
 Family history
 in diagnostic workup, 363-364
 in prediction of hypertension, 30, 42
 Family support, 396, 407
 Feasibility trials, *see* Clinical trials; *specific studies*
 Fibrinoid arteriolar necrosis, 128
 Follow-up visits, 295
 Food and Drug Administration, U.S., 250, 320
 Framingham Heart Study, 70, 129, 130, 140, 340, 426, 427, 447
- G**
 Glucose intolerance, 152
 Group d'Etudes sur l'Epidemiologie de l'Atherosclerose (GEEA), 310, 311
 Guanethedine sulfate, 91, 93, 96
- H**
 Health and Nutritional Examination Survey, 425
 Health beliefs, patient compliance and, 395-396, 405
 Health education, patient compliance and, 399-400, 405-406
 Heart failure, 61-62
 Heart rate, 42
 Hemodynamic heterogeneity, 34
 Hi-Blood Program, 463-465
 High density lipoprotein (HDL), 130-131
 High-renin hypertension, 161-163, 166-167
 Howard University Hospital Family Planning Clinic, 366
 Hydralazine, 118, 163
 adverse effects of, 91, 92
 Hypercholesterolemia, 142-143
 Hyperkinetic state, 47-48
 Hypertension Detection and Follow-up Program (HDFP), 7, 99, 222, 247, 249, 250, 254-264, 309-311, 443, 444
 design of, 289, 292
 drug regimen in, 291-292
 ethical considerations in, 415-416
 Hypertension Education Program, 460
 Hypertension Pretreatment Data Base, 376-379
 Hypertension Screening and Treatment Program, 463
 Hypertensive evaluation, 368-369
 Hypertensive personality, 101, 225
 Hypokalemia, 223
 Hypotensive drugs, *see* Antihypertensive drugs
- I**
 Iatrogenic complications, 62-64, 123-124, 275
 Impotence, 120-121, 290
 Infant mortality, 203
 International Atherosclerosis Project, 140
 International Society of Hypertension, 311, 458
 Inter-Society Commission for Heart Disease Resources, 337, 352, 363
 Intravenous pyelogram, 369-370
 Isometric exercises, 224
 Isotonic exercises, 224
- J**
 Joint National Committee on Detection, Evaluation and Treatment of Hypertension, 80, 304, 331, 374
- K**
 Kaiser-Permanente Health Plan Clinics, 102
 Kempner rice diet, 201, 223
 Kidneys
 blood pressure regulation by, 161
 natriuretic capacity of, 194-195
 salt intake and, 180-181, 183-186, 194

Labile hypertension, 58Laboratory evaluation, 377, 379
in diagnostic work-up, 367-368

Latent disease, 374, 379

Lead in water supply, 204, 206-207, 211

Left ventricular hypertrophy, 79

Lipids, 128-139

Lipoproteins, 130-134

Los Angeles Civil Servant Study, 140

Low-renin hypertension, 161-163, 166-167

Magnesium

in diet, 213-215

in water supply, 211, 213-215

Malignant hypertension

aldosterone production in, 162

renin and, 167

Malignant neoplasm, 203

Mass treatment, 333-362

comprehensive care in, 347-348

defining candidates for, 333-336

medical practice and, 348-354

nonpharmacologic approaches to, 340-346, 359-360

pharmacologic treatment in, 346-347, 359

pretreatment measures in, 336-340

Medical history, 363-365, 376-377

Medical Research Council, 290, 422

Men of 1913 study, 140

Methyldopa, 163

adverse effects of, 89-90, 96

national consumption patterns of, 326-327

Midwest Railroad Study, 140

Mild hypertension

benefit of treatment for, 68-72

complications of, 59-64, 66

definition of, 3-17

diagnostic work-up for, 363-370, 373-380

intervention trial in, 74-80

as sign of latent disease, 374-375

See also Borderline hypertension; Essential hypertension

Mild Hypertension Study, 464

Mineralocorticoid hypertension, 181

Minnesota Business and Professional Men's Study, 140

Mortality, 8-10, 16

systolic blood pressure and, 334

water hardness and, 203, 211-215

Multiple Risk Factor Intervention Trial (MRFIT), 293-304, 309, 443, 444, 450, 452, 454

Multiple logistic function, 303

Multirisk factor analysis, 151-152, 157

Myocardial infarction, 76-79, 290

National Health Survey, 4, 29, 42

National Blood Pressure Study (NBPS), 155, 310, 311

National Cancer Institute, 244

National Cooperative Pooling Project, 9, 140

National Cooperative Study on Renovascular Hypertension, 364

National Heart Institute, 244

National Heart and Lung Institute, 99, 363, 414, 415

National Heart, Lung and Blood Institute, 21, 26, 28, 222, 254, 267, 373
clinical trials by, 441-457*See also* Veterans Administration-National Heart, Lung and Blood Institute study

Hypertension Education Program of, 460

National High Blood Pressure Education Program, 72, 324, 354, 363, 381, 384, 454, 455

National Institutes of Health (NIH), 441-451

Nephritis, 203

"Neurogenic" borderline hypertension, 45-46

Neurohumoral heterogeneity, 34

Nitrates, 204-205, 211

Non-drug management, *see* Non-pharmacologic treatment

"Non-neurogenic" borderline hypertension, 46

Non-pharmacologic treatment, 80, 222-242, 340-346

behavior modification in, 224-232, 239-240

diet in, 223

physical exercise in, 223-224, 237-239, 241

salt restriction in, 240-241

Norsk Medisinaldepot, 321

Nutritional therapy, 378-379

See also Diet**O**besity, 30, 53, 108, 223, 259, 262

control of, 331, 360

in mass treatment, 340-346

Obesity
 in prediction of hypertension, 42
 prevention of hypertension and, 461-462

Optic fundus, 366

Oral contraceptives, 365-366

Packaging of medications, 401
Paramedical personnel, 381-389
Patient behavior, 99-101
Patient compliance, 2, 109, 231-232, 332, 337-340, 347, 390-402, 404-407, 410-411
 clinical significance of, 393-394
 cost-effectiveness and, 430-431
 health beliefs and, 395-396
 measurement of, 391-392, 404-405
 socioeconomic factors in, 411
 strategies to improve, 397-402

Peoples Gas Company study, 333, 340, 341

Peripheral resistance, 191-194

Personality assessment, 101

Pharmacologic treatment, *see* Antihypertensive drugs

Pheochromocytoma, 365, 367

Physical examination, 366

Physical exercise, *see* Exercise

Placebo effect, 107, 225

Placebo trials, ethical considerations in, 415, 422-423

Plasma renin activity
 antihypertensive drugs and, 167
 determination of, 368-369
 in reduction of cardiovascular risk, 147, 149

Potassium, 198-201
 in diet, 361

Prazosin hydrochloride, 92, 94

Prediction of hypertension, 38-58
 by descriptive characteristics, 41-42
 multiple factors in, 42-44
 by provocative tests, 40-41
 renin and, 147-157, 161

Pregnancy, 71, 365

Pretreatment data base, 376-379

Prevention of hypertension, 239-242, 461
 exercise in, 241
 primary, 355-356
 salt restriction in, 240-241
 weight control in, 239-240

Preventive medicine team, 387

Primary aldosteronism, 163, 365, 367

Primary endpoints, 76-77, 247

Primary hypertension

 aldosterone production in, 162
 atherosclerosis and, 128-130
 childhood precursors of, 28-37

Primary prevention, 355-356

Primitive societies, 107-108

salt intake in, 178-179, 198-200, 223

Private practice, outcome evaluation of, 386

Progesterone levels, 161

Propranolol, 64, 66

 adverse effects of, 90, 91

 as renin inhibitor, 163, 164

Prostaglandins, 161

Provocative tests, 40-41, 48-49

Psychological factors, 41, 42

Psychosocial factors, 101-104

Psychotherapy, 225, 231

Public Health Service, U.S., 115, 117

Race factors, 256-259, 261
 antihypertensive therapy and, 70, 71
 blood pressure and, 297-299
 body weight and, 239
 plasma renin activity and, 151-154
 in prediction of hypertension, 42
 rate of hypertension and, 102-103
 renovascular hypertension and, 364
 See also Blacks

Rauwolfia alkaloids, 325-328

Relaxation therapies, 227-231

Renal hormone levels, 161

Renal papillary plasma flow, 186-191, 194

Renal parenchymal disease, 183, 364, 370, 374

Renin, 46, 161-164

 inhibitors and stimulators of, 163
 as predictor of cardiovascular damage, 166

 as risk factor, 149-156

 as vasculotoxic agent, 147-148

 vasoconstriction induced by, 165-166

Renin-dependent hypertensive disease, 149

Renin-sodium profiling, 165-173

Renovascular hypertension, 167, 364-365

Reserpine, 118, 163, 290, 328

 adverse effects of, 87-88, 96

 drug interactions with, 88-89

Response to exercise, 40-41

Risk factors, 164, 303

 in coronary heart disease, 293, 297-299

 of drug side effects, 397, 410-411

 duration of therapy and, 365

- Risk factors
family support and, 396
health beliefs and, 395-396, 405
in patient noncompliance, 394-397
renin as, 149
Roentgenographic evaluation, 367-368
- S**
St. Thomas' Hospital Trial, 310, 315
Salt intake, 108-110, 163, 178-195
blood pressure and, 198-199
from drinking water, 206-207
eating habits and, 361-362
epidemiologic studies of, 178-179, 207-208
experiments on, 178-185
kidneys and, 180-181, 183-194
prevention of hypertension and, 240-241, 461-462
renin and, 149
restriction of, 223, 360
See also Sodium
Salt loading, 55
Salt taste threshold, 200
Screening, 268-272, 281-283, 291, 293-297
cost-effectiveness of, 432-434
Self-monitoring, 400
Sex factors
antihypertensive therapy and, 70, 71
in clinical trials, 291
systolic pressure and, 33
Serum cholesterol, 130-131, 140, 142, 152, 259, 262, 293, 297-298
Side effects, 283-286
adverse, 84-98
patient compliance and, 100-101, 410-411
placebo effect and, 107
Seven Countries Study, 240
Society of Actuaries, 8
Socioeconomic factors, 101-104
in patient compliance, 411
Sodium
antihypertensive drugs and, 167-168
calcium and, 207
regulation of blood pressure by, 161
water softening and, 208
in water supply, 204, 211
See also Salt intake
Sodium retention, 163
Soft water, 208
"Soldier's heart," 469-470
Spironolactone
adverse effects of, 86-87
extracellular fluid volume and, 183
Stepped care, 254-256, 261-262, 296
Stress, 41, 101-104, 109
socioeconomic conditions and, 360, 440
Stroke, 76-78, 139
blood pressure level and, 157
decline of mortality from, 146
vasoconstriction and, 165
Suprabulbar projections, 33-34
Systolic blood pressure
mortality and, 334
risk of coronary heart disease and, 135
- T**
Target organ damage, 74, 259, 263
assessment of, 164
in definition of hypertension, 4, 12
intervention and, 11
Tecumseh Study, 140
Therapeutic compliance, *see* Patient compliance
Therapeutic trials, *see* Clinical trials
Thiazides, 64, 290, 368
adverse effects of, 85-86, 96, 98, 144
drug interactions with, 86, 96
effect on myocardial infarction of, 290
extracellular fluid volume and, 183
Tracking correlations, 30, 36
Transient hypertension, 58
Transport Workers Study, 140
Treatment Trial for Mild Hypertension, 310, 311, 315
Triamterene, 87, 88
Triglycerides, 130
- U**
Urinalysis, 374, 377, 379
Urine sodium measurement, 165
Utility function, 112-127
- V**
Vasculotoxic agents, 147-148
Vasoactive agents, 148
Vasoactive kinins, 161
Vasoconstriction
extracellular fluid volume and, 182
renin-induced, 165-167
salt intake and, 185, 194
Very low density lipoproteins (VLDL), 130-131
Veterans Administration, 267, 463-464
Veterans Administration Cooperative Study, 10, 15, 38, 60, 72, 111, 115, 117, 118, 165, 222, 250, 254, 267, 309, 373, 414-415

Veterans Administration Cooperative Study

comparison of PHS Hospitals Trial and, 75, 76, 79

coronary heart disease in, 137, 144-145

limitations of, 69-71

significance of, 68-69

Veterans Administration-National Heart, Lung and Blood Institute Feasibility Trial, 310

administration of, 277-280

data management in, 276-277

design of, 289-292

iatrogenic events in, 275

loss to study in, 275-276, 285, 286

morbidity events in, 275, 283-286

sample size for, 267-268

screening in, 268-272, 281-283, 291

study population criteria for, 269

treatment in, 272-276, 283

Volume excess hypertension, 167

Water hardness, 204

cardiovascular disease and, 211, 220-221

epidemiology of hypertension and, 208-210

mortality and, 203, 211-215

Weight control, 239-240

See also Obesity

Western Collaborative Group Study, 140

Western Electric Company Study, 59-61, 340, 341

Whitehall Study, 140

Women

in clinical trials, 291

in Public Health Survey, 83

risk of coronary heart disease in, 135

See also Sex factors

World Health Organization, 7, 311, 321, 458

Zinc, 211



Author Index

(Italicized page numbers refer to comments in Discussions)

Agnati, Luigi F., 346-369

Baldessarini, Ross J., 198-206
 Baliga, B. Suren, 96-105
 Barofsky, A.-L., 174
 Baumgarten, H. G., 3-24, 36-56, 56, 84, 94, 107-117, 117-118, 133, 145, 171, 175-177, 189, 206, 258, 260-261, 262-288, 423-436
 Björklund, Anders, 3-24, 305-327, 370-384
 Bobillier, P., 576-589
 Bonetti, E. P., 595-620
 Bosin, Talmage R., 134-145
 Breese, G. R., 160-170, 171-174, 241, 260, 664-665 (Moderator), 664
 Browning, Ronald A., 437-456, 456
 Bruckwick, Eleanor, 182-188

Campaigne, Ernest, 134-145
 Campbell, Alexander, 198-206
 Carruba, Michele O., 172, 242-258, 258, 478
 Clemens, James A., 399-410, 410, 478
 Clineschmidt, Bradley V., 222-241, 241
 Cohen, Gerald, 74-84, 84
 Collu, Robert, 411-422, 422
 Coscina, Donald V., 172, 206, 241, 456, 479, 627-644, 664-665
 Creveling, C. R., 56, 57-73, 145

Da Prada, M., 56, 118, 146, 173, 260, 385, 595-620, 665
 Donelson, Alan C., 134-145
 DuCret, R. P., 590-594

Fuller, Ray W., 147-157, 158-159, 172, 175-177, 178-181, 241, 259-261 (Moderator), 260
 Funderburk, W. H., 302-303
 Fuxe, Kjell, 346-369, 386

Gál, E. M., 84, 105, 119-127, 127, 158-159, 175-176, 241

Gargiulo, Giuliana, 242-258
 Gershon, M. D., 385
 Gerson, Sylvia C., 198-206
 Giambalvo, C. T., 173-174, 189, 478, 524-531, 589, 664
 Göthert, Manfred, 457-476, 477
 Growdon, John H., 159, 207, 510-523
 Gustafsson, Jan-Åke, 346-369

Hallman, H., 328-345
 Hancke, J. L., 423-436
 Harvey, John A., 259, 289-302, 303-304, 385-386 (Moderator), 385, 664-665
 Heikkilä, Richard E., 74-84, 133
 Hoebel, B. G., 478-479, 590-594
 Hoffman, William E., 437-456
 Höhn, K. G., 423-436
 Horn, A. S., 128-133, 133, 158

Jacobs, Barry L., 207, 479, 497-509, 664
 Jacoby, Jacob H., 1-2, 146, 258, 261, 387-398, 478-479 (Moderator), 478, 664
 Jonsson, G., 328-369, 665
 Jouvett, M., 576-589

Kaufman, Nathan, 480-496
 Keane, P., 576-589
 Keller, H. H., 595-620
 Klemm, H. P., 3-24, 36-56, 107-117
 Klupp, Niels, 457-476
 Köhler, Christer, 385, 645-663

Lachenmayer, L., 3-24, 107-117, 262-288, 385
 Lorens, Stanley A., 532-535, 665
 Lovenberg, W., 3-24, 182-188, 188-189, 221
 Lundberg, J. J., 262-288
 Lytle, Loy D., 1-2, 175-177 (Moderator), 480-496

McGinty, J., 241, 385
 McGuffin, Jodie C., 222-241

MacKenzie, R. G., 590-594
Maickel, Roger P., 134-145, 145-146
Massari, V. J., 259
Meek, James L., 190-196, 259, 261
Meshul, C. K., 84, 221
Messing, Rita B., 480-496
Meyer, J., 410, 422
Møllgård, K., 262-288
Moskowitz, Michael A., 96-105, 105-106, 259
Mueller, R. A., 160-170
Munro, Hamish N., 96-105
Myers, R. D., 385, 478, 556-575, 665

Natelson, B., 479
Nisticò, Giuseppe, 242-258
Nobin, Anders, 305-327, 370-384, 385
Norelli, C., 590-594
Nowak, Thaddeus S., Jr., 96-105

Ögren, Sven-Ove, 346-369, 645-663

Pettibone, Douglas J., 480-496
Pflueger, A. Barbara, 222-241
Pieri, L., 595-620
Pieri, M., 595-620
Pollare, T., 328-345
Pujol, J. F., 478, 576-589, 589, 664

Radulovacki, M., 146, 196-197
Rapport, Maurice M., 85-94
Reinhard, J. F., Jr., 476
Renaud, B., 576-589
Rogers, Richard B., 134-145
Ross, Svante B., 645-663

Rotman, A., 57-73
Rubin, Deborah, 96-105

Sachs, Ch., 328-345
Sanders-Bush, Elaine, 127, 158, 175-176, 208-221, 221, 260
Sankar, Dr., 95
Schlossberger, H. G., 3-35, 107-117
Sherman, A. D., 119-127
Silbergeld, E. K., 95
Simonton, Ronald L., 437-456
Smith, G., 422
Snodgrass, S. R., 524-531
Sperk, Günther, 198-206
Srebro, Bolek, 645-663
Stein, J., 260
Steranka, Larry R., 208-221
Stewart, R. Malcolm, 198-206, 206-207, 260-261, 410

Tamir, Hadassah, 56, 73, 85-94, 94-95, 171, 188, 422
Thomas, Ronald F., 387-398
Totaro, James A., 222-241
Trulson, Michael E., 497-509, 590-594, 664

Uretsky, N. J., 524-531

Wiklund, Leif, 262-288, 370-384
Wishousky, Theodore I., 222-241
Wuttke, W., 410, 423-436, 479

Zacchei, Anthony G., 222-241
Zemlan, Frank P., 590-594, 621-626

Subject Index

Italicized page numbers refer to material in figures or tables.

The list of terms which precedes the index proper was adhered to strictly to bring about consistency in constructing the index. Under each chosen term are various synonyms, initialisms, etc. each preceded by "=". The reader is cautioned to check here for the various alternatives which may occur in the text itself, as different authors may use different terms. None of the alternatives appear in the index itself as references, because they may not have been needed alone as main headings and/or subheadings under other main headings.

- N*-Acetylnorfenfluramine
 - =FE₃
- Adrenocorticotrophic hormone
 - =ACTH
- Amine precursor uptake decarboxylase
 - cells
 - =APUD cells
- 6-Aminodopamine
 - =6-ADA
- 3-(β -Aminoethyl)-5,6-dihydroxybenzo[*b*]-thiophene
 - =5,6-DHT-S
- 3-(β -Aminoethyl)-5,6-isopropylindenoxybenzo[*b*]thiophene
 - =IPST
- Aurintricarboxylic acid
 - =ATA
- Avoidance behavior
 - =CAR
 - =Conditioned avoidance response
- Bacterial pyrogen
 - =Pyrifer® VII
- p*-Bromoamphetamine
 - =*p*-BA
 - =4-Bromoamphetamine
- Catechol *O*-methyltransferase
 - =COMT
- Catecholamines
 - =CA
- p*-Chloro-*N*-methylamphetamine
 - =*p*-CMA
- p*-Chloroamphetamine
 - =*p*-CA
 - =*p*-Chloro- α -methylphenylethylamine
 - =4-Chloroamphetamine
- p*-Chloronorephedrine
 - =*p*-Chloro- β -hydroxyamphetamine
 - =P₂
 - =PCNE
- p*-Chlorophenylalanine
 - =*p*-CPA
- Chromatography, high-pressure liquid
 - =HPLC
- Desmethylinipramine
 - =Desipramine hydrochloride
 - =DMI
 - =Norpramin®
- Deuterium oxide
 - =D₂O
 - =Heavy water
- 5,6-Diacetoxytryptamine
 - =5,6-DACOT
- 5,6-Dihydroxyindoleacetic acid
 - =DHIAA
- 5,6-Dihydroxytryptamine
 - =5,6-DHT
 - =5,6-HT
- 5,7-Dihydroxytryptamine
 - =5,7-DHT
 - =5,7-HT
- 3,4-Dimethoxyamphetamine
 - =3,4-DMA
 - =P₃
- 6,7-Dimethyl-5,6,7,8-tetrahydropterine
 - =DMPH₁
- Dopa
 - =Dihydroxyphenylalanine
 - =DOPA
- L-Dopa
 - =Levodopa
- Dopa decarboxylase
 - =DDC
- Dopamine
 - =DA
- Dopamine β -hydroxylase
 - =DBH
- Fenfluramine
 - =*N*-Ethyl- α -methyl-3-trifluoromethyl- β -phenylethylamine
 - =*N*-Ethyl- α -methyl-*m*-(trifluoromethyl)phenylethylamine
 - =FE
 - =FEN
- p*-Fluoroamphetamine
 - =4-Fluoroamphetamine

- Fluoxetine
 = FLU
 = Lilly 110,140
 = 3-(*p*-Trifluoromethylphenoxy)-*N*-methyl-3-phenylpropylamine
 Follicle-stimulating hormone
 = FSH
 Glutathione, reduced
 = GSH
 Growth hormone
 = GH
 = Pituitary growth hormone
 = Somatotropin
 = STH
 Harmaline
 = HAR
 Homovanillic acid
 = HVA
 5-Hydroxy-6-methoxytryptamine
 = 5-H-6-MT
 6-Hydroxydopamine
 = 6-HD
 = 6-OHDA
 = 2,4,5-Trihydroxyphenylethylamine
 5-Hydroxyindoleacetic acid
 = 5-HIAA
 Hydroxyl radicals
 = $\cdot\text{OH}$
 2-[β -(4-Hydroxyphenyl)ethylamino-methyl]tetralone
 = HEAT
 6-Hydroxytryptamine
 = 6-HT
 5-Hydroxytryptophan
 = 5-HTP
 Isoprenaline
 = Isoproterenol
 Lisuride maleate
 = Lysenyl®
 = Lysuride acid maleate
 Lu 10-171
 = 1-(3-Dimethylamino)propyl-1-(*p*-fluorophenyl-5-phthalan carbonitrile hydrobromide
 Luteinizing hormone
 = LH
d-Lysergic acid diethylamide
 = LSD
 Maprotiline
 = MAP
 Maximal velocity
 = V_{\max}
 Melanocyte-stimulating hormone
 = MSH
 5-Methoxy-*N,N*-dimethyltryptamine
 = 5-MDMT
 3-Methoxy-4-hydroxyphenylethylene-glycol
 = MOPEG
 3-Methoxy-4-hydroxyphenylethylene-glycol sulfate
 = 3-Methoxy-4-hydroxyphenylglycol sulfate
 = MOPEG-SO₄
 5-Methoxy-6-hydroxytryptamine
 = 5-M-6-HT
 α -Methyl-5-hydroxytryptamine
 = α -Methyl-5-HT
 = Serotonin, α -methyl
 Michaelis constant
 = K_m app
 Monoamine oxidase
 = MAO
 Monoamine oxidase inhibitors
 = MAOI
 Norepinephrine
 = NA
 = NE
 = Noradrenaline
 Norfenfluramine
 = NFE
 = *m*-Trifluoromethylamphetamine
 Pentylene tetrazol
 = PTZ
 Perchloric acid
 = PCA
 Peroxidase, horseradish
 = HRP
 1-Phenyl-3-(2-thiazolyl)-2-thiourea
 = PTTU
 Piperocaine
 = Metycaine®
 Prolactin
 = LTH
 = Luteotropin
 = Pituitary lactogenic hormone
 Reserpine
 = RES
 Ribonucleic acid
 = Messenger RNA
 = RNA
 Serotonin
 = Enteramine
 = 5-HT
 = 5-Hydroxytryptamine
 Serotonin-binding protein
 = SBP
 Subcommissural organ
 = SCO
 Thyroid-stimulating hormone
 = Thyrotrophin
 = Thyrotropin
 = TSH

m = Trifluoromethylbenzoylglycine

=FE₂

Tritium

=³H

=T

Tryptophan

=TP

Tyrosine hydroxylase

=TH

Zimelidine

=(z)-3-Dimethylamino-1-(4-bromo-phenyl)-1-(3-pyridyl)propene

=H 102/09

- A** cetazolamide
 effect of 5,7-dihydroxytryptamine or a raphe lesion on anticonvulsant action, 448—450, 452
 effect on maximal electroshock-induced hindleg extension in rats, 449, 449, 450
 after a raphe nuclei lesion, 450, 450
- Acetylcholine, 519
 effect of *p*-chloroamphetamine on, 260
 raphe lesion lowering forebrain concentration, 453
- Acetylcholinesterase, 538
- N*-Acetylnorfenfluramine, 120, 125—126
- Activity level, 542—543
 effects of
 5,7-dihydroxytryptamine, 544
p-chloroamphetamine, 543—544
p-chlorophenylalanine, 543
 selective raphe lesions, 543
 novel vs. familiar environment, 543
- Adenosine triphosphate
 as inhibitor of serotonin-binding protein capacity, 91
- Adrenal gland, 392
- Adrenal-pituitary axis. *See* Pituitary-adrenal axis
- Adrenal steroids
 blocked by dexamethasone, 621, 622
 release stimulated by serotonin or 5-hydroxytryptophan, 392
- Adrenalectomy, unilateral
 and depletion of serotonin with *p*-chlorophenylalanine, 392
- Adrenergic receptors, α - and β -, 391, 458
 β -antagonists. *See* Pindolol
- Adrenocorticotrophic hormone, 391—393
 hypersecretion occurring after lesions of ascending serotonin pathways, as shown by increased basal corticosterone secretion, 362
- Aggressive behavior
 more prevalent in rats pretreated with *p*-chlorophenylalanine than 5-hydroxytryptophan, 486
- Aldehyde dehydrogenase, 18
- Amine precursor uptake decarboxylase cells, 284
- Amines
 influence of various antagonists on positive chronotropic effects in guinea pig right atria, 462, 464
- 6-Aminodopamine, 76—77
 mechanism of action, 80
- 3-(β -Aminoethyl)-5,6-dihydroxybenzo[*b*]-thiophene
 ability to lower stored norepinephrine, 143
 and behavioral changes in rats, 136, 139—140
 stability, 145
- 3-(β -Aminoethyl)-5,6-isopropylindendioxibenzo[*b*]thiophene
 biochemical and behavioral effects in rats, 140—141
- d*-Amphetamine, 479, 510, 527—531, 542
 and brain serotonin concentration, 92
 and protein synthesis, 105—106
 effect on protein synthesis, 101—104
 effects, 251—252, 254—256
 hyperthermia induced by, 252, 254—256
 increased responsiveness to, 385—386
- Amphetamines, halogenated. *See* Halogenated amphetamines
- Anorexia, 484—485. *See also* *p*-Chloroamphetamine; *p*-Chlorophenylalanine and serotonin; Fenfluramine; Fluoxetine
 amphetamine-induced in rats, 593
 fenfluramine-induced enhanced after 5,7-dihydroxytryptamine treatment in rats, 593—594, 593
- Antimycin A and oxygen consumption, 81
- Apomorphine, 389, 391, 479, 510, 524, 527—531, 596, 605, 613, 615
 inducing locomotor activity and stereotyped behavior in rats, 348
 ineffective in producing myoclonic syndrome in rats, 511
 stimulation of dopaminergic receptors to cause hypothermia or hyperthermia, 252
- Aromatic amino acid decarboxylase inhibitors. *See* RO4-4602
- Ascorbic acid depleted by serotonin or 5-hydroxytryptophan, 392
- Atropine, 515, 518, 529
- Aurintricarboxylic acid
 effect on polysomal profiles, 102, 103
 effect on protein synthesis, 101—102, 101
- Avoidance behavior, 544—545
 5,6-dihydroxytryptamine effects, 544
 5,7-dihydroxytryptamine effects, 544—545
 by rats, 657—658, 658
 discriminated, 545
 one-way, signaled or unsignaled, 545
p-chloroamphetamine effects, 544—545
p-chlorophenylalanine effects, 544—545
 selective raphe lesion effects, 544
 two-way (shuttle), 544

Bacterial pyrogen, 254Behavior. *See also* Aggressive behavior;

Avoidance behavior; Behavior, rotational; *p*-Chloroamphetamine; Crossing behavior of rats; 5,6-Dihydroxytryptamine—and behavioral changes; Locomotor activity; *d*-Lysergic acid diethylamide-induced behavioral syndrome in rats; 5-Methoxy-6-hydroxytryptamine; Mounting behavior; Rearing activity; Seizure susceptibility changes; Sexual behavior

as determined by injection of 5,7-dihydroxytryptamine in rats, 347—349, 366

changes and percent reductions in regional serotonin concentrations after discrete electrolytic brain stem lesions, 533, 534, 537, 542, 544

contacts with objects by rats, 652, 652 effects of *p*-chloroamphetamine on rats, 658—660, 659

effects of serotonin depletion, 546, 547 exploration of field by rats, 654, 654, 655

possibly related to route by which 5,7-dihydroxytryptamine was injected into rats, 638, 640

scoring in rats, 514—515

studies with rats, 497, 649—658

Behavior, rotational

after nigrostriatal lesions in rats, 524

after serotonin-pathway lesions in rats, 529

after treatment with 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine in rats, 605, 608, 614—616

correlation between size of lesion in the median raphe nucleus and vigor of the rotation, 526

effects of serotonin neurotoxins in rats, 524—531

in rats, 596

injected rats tested with amphetamine, 524—526

injected rats tested with apomorphine, 524—526

time course, 526

Benserazide causing marked sexual stimulation in rats, 613

Benzodiazepine action over inhibitory γ -aminobutyric acidergic system and reduction of serotonin turnover, 363

Benztropine

effect on retention of radioactivity in rat brain, 108, 110, 114—116

4-Benzyloxy-5-methoxyindole synthesis, 25—26, 26

4-Benzyloxy-5-methoxytryptamine formate ultraviolet spectra, 29, 31

Blood platelets, 617

after incubation in plasma at 37°C, 597

from rabbits and guinea pigs, 615

serotonin content after incubation in plasma with 5,6-dihydroxytryptamine, 5,7-dihydroxytryptamine, or metaraminol, from rats, 609, 609

storage pool deficiency, 616

ultrastructural aspects after incubation in plasma with 5,6-dihydroxytryptamine, 5,7-dihydroxytryptamine, or metaraminol, from rats, 609, 610, 611, 616

Blood pressure, arterial

hypertension in rats, 471—472

pretreatment with neither reserpine nor cocaine decreased the pressor effect of 5,6-dihydroxytryptamine, 457, 459

pressor effect of 5,7-dihydroxytryptamine considerably less than of 5,6-dihydroxytryptamine, 458

Body temperature. *See* Temperature, bodyBody weight. *See* Weight, body

Brain. *See also* Hippocampus; Hypothalamus; Locus ceruleus; Serotonin—brain concentration; Serotonin—in brain

5-hydroxyindoleacetic acid content in rats, 649

areas B8 and B9, 623

bulbospinal system of rats, 372

regrowth, 377

content of monoamine metabolites after 5,7-dihydroxytryptamine injected intraventricularly in rats pretreated with desmethylimipramine, 597, 600, 613

diencephalon functionally analyzed for serotonin system, 347—349

dorsal accessory nucleus of the inferior olive of rats, 378, 380—381

enzymatic activity, 188—189

fluorescence histochemical studies in rats, 376—379

hypothalamus reactive to serotonin agonistic properties of quipazine, 390

Brain—(cont'd)

- inferior olive of rats, 377—379, 378
 - after administration of 5,6-dihydroxytryptamine, 379, 382
 - medial hypothalamic lesions
 - after 5,7-dihydroxytryptamine in rats, 640—642
 - or sham surgery with measures of food and water intake and body weight in rats, 627, 633, 633, 636, 638
 - midbrain raphe lesions in rats, 629, 641
 - midbrain stained with thionine showing lesion involving dorsal and median raphe nuclei in rats, 441, 441
 - pathology in rats, 631
 - raphe-lesioned rats for monoamine analyses, 444, 446, 447, 450, 451
 - schematic representation in rats, 329, 329
 - serotonin content, 665
 - decrease in rats, 503
 - in rats, 646—647, 649
 - in various regions after *p*-chloroamphetamine treatment in rats, 646—647, 647
 - increase in rats, 665
 - of B9 region, 297
 - uptake in different regions affected by *p*-chloroamphetamine and zimelidine plus *p*-chloroamphetamine, in rats, 647, 648
 - telencephalon functionally analyzed for serotonin system, 347—349
 - topography of area perfused with 5,6-dihydroxytryptamine in rats, 576, 577
 - tryptophan concentrations and 3-(β -aminoethyl)-5,6-dihydroxybenzo[*b*]-thiophene, 146
- Brain lesions. *See also* Behavior; Behavior, rotational; Dopamine; Norepinephrine
- of medial forebrain bundle in rats, 529
 - of substantia nigra, 527
 - relation with dopamine neurons, 524
- Brain metabolism of serotonin depletors, 119—126
- Brain mitochondria
- binding of radioactivity to after intraventricular injection of [¹⁴C]-5,6-dihydroxytryptamine and [¹⁴C]-5,7-dihydroxytryptamine, 11—12
 - interaction of 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine in rats, 74—75, 81—82, 81

- Brain stem serotonin and norepinephrine levels after 5,6-dihydroxytryptamine or 3-(β -aminoethyl)-5,6-dihydroxybenzo[*b*]thiophene in rats, 136, 138, 139
- p*-Bromoamphetamine, 150, 158, 178, 289—291, 296—297
- cf.* *p*-chloroamphetamine in exerting neurotoxicity, 176
- duration of reversibility of serotonin depletion, 148, 149, 154
- 2-Bromolysergic acid diethylamide, 203, 204
- blocking myoclonic syndrome in rats, 511
- p*-Bromomethamphetamine, 150
- Bufotenine as inhibitor of serotonin-binding protein capacity, 86, 88, 93

- C** cells of thyroid. *See* Thyroid C cells
- Carbidopa to block 5-hydroxytryptophan effects, 410
- Carbonic anhydrase inhibitors, 438, 452
- Castration
 - did not affect mounting behavior in male rats, 603
 - of rats, 486
- Catalase
 - inhibition of tryptamine conversion not antagonized, 41
- Catechol *O*-methyltransferase, 17, 19, 36, 53
- Catecholamine neurons, 600
 - effect of 5,6-dihydroxytryptamine on, 346
- Catecholamines, 254—255, 540, 542, 586—587, 613, 616, 631
 - behavioral tolerance, 212
 - effect of *p*-chloroamphetamine on, 209
 - fluorometric estimation in brain, 244
 - histofluorescence, 244
 - metabolism, 212
 - uptake blockers. *See* Desmethylinipramine; Protriptyline
- Centrally acting drugs. *See* Drugs, Centrally acting
- Cerebrospinal fluid
 - circhoral luteinizing hormone pattern in ovariectomized injected rats, 427, 431
 - serum luteinizing hormone, prolactin, and monoamine levels in ovariectomized rats treated in hypothalamus, 427, 428
- Chlorimipramine, 289, 372—373, 373, 374—375, 376

- Chlorimipramine—(cont'd)
 and serotonin-binding protein, 95
 and serotonin uptake, 222
 blocking of anorectic effects of fenfluramine, 241
 blocking of uptake of 5,7-dihydroxytryptamine into adrenergic sites, 56
 inhibiting serotonin transport, 20
 inhibiting tyrosine hydroxylase activity increase in locus ceruleus by 5,6-dihydroxytryptamine treatment in cats, 584—585, 585
 pretreatment as a control for 5,7-dihydroxytryptamine in rats, 349
 unavailable to protect serotonin fibers from 5,6-dihydroxytryptamine, 613
- 6-Chloro-2-aminotetralin, 153—154
- p*-Chloro-*N*-methylamphetamine, 147, 224, 546
- m*-Chloroamphetamine, 150, 154
- o*-Chloroamphetamine, 150
- p*-Chloroamphetamine, 147, 158—159, 178—179, 289—291, 296—297, 302—304, 385—386, 403, 481—486, 488—490, 511, 514—515, 529—530. *See also* in subheads under other main headings, e.g. Avoidance behavior—*p*-chloroamphetamine effects
- abnormal behavior production, 212—213
- administration, 123
- and amino acid incorporation, 105—106
- and concentration of serotonin and tryptophan hydroxylase in brain nuclei, 190
- and glutathione levels, 215
- and neurotoxicity, 153—154
- and reduced glutathione in brain, 121, 123
- and sexual behavior in female rats, 621
- and tryptophan 5-hydroxylase activity, 126
- brain concentration after injection of *p*-chloroamphetamine or *p*-chloro-*N*-methylamphetamine in rats, 150—151, 151
- cf. fenfluramine, 239
- correlation between turnover decrease in cortical serotonin and increase in striatal dopamine in rats injected unilaterally into median raphe nucleus or substantia nigra, 526—527, 527
- early changes in norepinephrine and dopamine and dynamics after injection, 209, 210
- effect in newborn animals, 172
- effect of acute drug treatment on the postural syndrome induced in rats, 515, 517, 519
- effect of fluoxetine on serotonin decreases after injection, 214, 214
- effect of increasing doses on the postural syndrome induced in rats, 515, 518
- effect of pretreatment with cysteine or diethylmaleate on long-term effect, 215-216, 216
- effect on
 mast cells and enterochromaffin cells, 385
 mating behavior induced by estradiol benzoate in female rats, 621, 622
 proestrous surges of luteinizing hormone and prolactin in female rats, 402, 402
 serum levels of luteinizing hormone, prolactin, and growth hormone in male rats, 400, 401, 409
- effect on brain
 B9 region in rats, 290—291, 292—293, 294
 B9 region in rats pretreated with fluoxetine, 292, 294
 serotonin, norepinephrine, and dopamine in rats, 291, 291
- effect when injected into median raphe nucleus in rats on serotonin and 5-hydroxyindoleacetic acid levels and serotonin and norepinephrine uptake, 525—526, 525
- fluorescence histochemistry of neurotoxic action, 357-358, 357
- hypothalamus and spinal cord resistant to depletion of serotonin after administration, 213
- in discrete brain nuclei, 191—192
- inducing anorexia, 478
- influence of administration route on brain levels, 120, 120
- influence on brain concentration of serotonin and 5-hydroxyindoleacetic acid, 148, 148
- inhibition of protein synthesis, 103—104
- injection effect on motor activity in rats, 210, 211
- injection increasing dopamine turnover, 589
- injection of rats, 515, 516

p-Chloroamphetamine—(cont'd)

interaction with fluoxetine in mice,
216, 217

long-term biochemical and behavioral
effects in rats, 645-660

long-term biochemical effects, 213-216

long-term neurotoxic effect on mating
behavior and forebrain monamine
levels in female rats, 621, 622

mechanism of action, 177

metabolism, 126

metabolite accumulation after brain
injection, 120, 121

neurotoxic effects, 259, 480

neurotoxic metabolites and age of ani-
mals, 175-176

neurotoxicity, 125, 127, 175, 186-187,
261

producing decrease in brain serotonin
and 5-hydroxyindoleacetic acid
content, 289

reduction of brain serotonin and 5-hy-
droxyindoleacetic acid, 119

reduction of resting levels of thyroid-
stimulating hormone in estrogen-
primed ovariectomized rats, 394

selective neurotoxic damage to the
brain, 351

Sidman avoidance, 211-212

species differences in mice and rats, 216

stereoisomers, 211

structure, 148, 149

subcellular distribution of metabolites
after brain injection, 121, 122

synaptosomal uptake of serotonin
after single injection, 213, 213

tolerance, 212

toxicity and metabolism, 215, 221

use to regulate body weight in human
beings, 485

p-Chloroamphetamine analogs, 152, 154

See also 3-Phenylpiperidines,
chlorinated

isomers, 158

structure, 148, 149

p-Chloroamphetamine and serotonin ac-
tions on serotonin neurons, 141-
142, 153-154

attempts to increase serotonin depletion
by, 192-193

changes in central serotonin neurons,
284

depletion of serotonin, 259

duration of reversibility of serotonin
depletion, 148, 149, 154

effect on brain serotonin content when
p-chloroamphetamine neonatally
administered in rats, 163-164,
164

effect on content of brain regions in
rats, 292, 295

effect on peripheral stores, 260

effect on serotonin neurons, 208

newborn rat brain serotonin, 241

reduction of brain serotonin in rats,
390-391

p-Chloroamphetamine homologs, 152

p-Chloromethamphetamine, 187

biochemical effects, 213, 217

tissue distributions of, 177

p-Chloronorephedrine, 126

metabolite of *p*-chloroamphetamine in
brain, 120

none detectable in brain or liver after
administration of iprindole, 124

p-Chlorophenylalanine, 145-146, 217,
388-389, 391-393, 405-406,
409, 444, 456, 487-488, 498, 515,
519, 532, 578, 590, 596, 664. *See*
also in subheads under other main
headings, e.g. Avoidance behavior
—*p*-chlorophenylalanine effects

and supersensitivity, 258

chronic administration did not in-
duce to various compounds, 503

lacking, 505

effect on brain monoamine concentra-
tions in rabbits, 247, 249

effect on growth hormone secretion in
rats, 422

failure to block suckling-induced pro-
lactin release, 433

in discrete brain nuclei, 193-194

induction of transient hyperphagia, 627

lowering of body temperature, 478

may increase locomotor activity in rats,
659

microinjection in rats, 571

mounting behavior in male, female,
castrated, and ovariectomized rats
alone or in combination with 5-
hydroxytryptophan or haloperidol,
603, 603, 614

pretreatment with neither enhances nor
antagonizes 5,7-dihydroxytrypt-
amine-induced hypothermia in
rats, 489

preventing rather than enhancing
audiogenic seizures in mice, 438

- p*-Chlorophenylalanine and serotonin
 blockade of central nervous system
 serotonin synthesis, 242—243, 252,
 254—256
 blockade of central serotonin syn-
 drome, 212
 depleting brain serotonin content, 510
 effect on serotonin in brain nuclei, 194,
 195
 inducing reductions in brain serotonin
 associated with insomnia, 483
 inhibiting serotonin synthesis, 423, 437
 inhibiting tryptophan hydroxylase, de-
 pleting brain serotonin causing
 reduction in food intake and loss
 in body weight, 556
 mechanism of action of serotonin neu-
 rons, 259
p-chlorophenylalanine decreasing brain
 serotonin biosynthesis and causing
 anorexia and hypodipsia, 484
 reduction of brain serotonin in rats, 390
 serotonin and tryptophan hydroxylase
 concentration in brain nuclei, 190
 total insomnia following inhibition of
 serotonin biosynthesis, 576
- p*-Chlorophenylalanine methyl ester hy-
 drochloride, 479
 brains injected later with fluoxetine in
 rats, 229, 233
- Chlorpromazine and prevention of lethal
 hyperthermia, 261
- Chlorpromazine effect on brain dopamine
 concentration, 173
- Cholesterol, 623—624
- Choline acetylase
 effect of *p*-chloroamphetamine on, 260
- Choline acetyltransferase, 538, 540
- Chromatography, high-pressure liquid,
 190—191
- Cinanserin as putative serotonin receptor
 antagonist, 485
- Cinanserin blockade of serotonin re-
 ceptors, 623
- Circadian rhythm, 587
- Clonidine, 391, 393
- Clorgyline, 48
- Clozapine as inhibitor of serotonin-bind-
 ing protein capacity, 92
- Cocaine, 462, 468, 471
- Cold environment, exposure to, 393—394
- Corpus striatum synaptosomes from rats,
 128
- Corticosteroids
 diurnal elevation in cats, rats, and man
 reduced by *p*-chloroamphetamine,
 393
- Corticosterone
 elevation after lesions of the raphe
 nuclei induced with 5,6-dihydroxy-
 tryptamine, 392
 suppressed by intraventricular or in-
 tracerebral injection of serotonin,
 392
- Covalent binding
 of 5,6-dihydroxytryptamine to atrial
 protein, 65
 of 5,7-dihydroxytryptamine to atrial
 protein, 65, 65, 71
 oxygen requirement for, 65, 67
p-chloroamphetamine or fenfluramine,
 127
- Covalent interaction of one or more ox-
 idation products of an amine with
 intraneuronal proteins, 57
- Cross-linking of protein
 oxygen dependency on, 68
 requirement for two active nucleophilic
 sites, 70
- Crossing behavior of rats, 656, 657
- Cushing's disease therapy, 392—393
- Cycloheximide, 203, 205, 207
- N*-Cyclopropyl-*p*-chloroamphetamine as
 inhibitor of monoamine oxidase,
 150—152
- Cyproheptadine, 284, 390, 462, 515,
 518—519, 539
 as blocker of serotonin receptors, 392
 as inhibitor of serotonin-binding pro-
 tein capacity, 91
 as serotonin receptor antagonist, 484
 pretreatment neither enhances nor an-
 tagonizes 5,7-dihydroxytrypt-
 amine-induced hypothermia in
 rats, 489
- Cytochrome P-450, 221
- Cytotoxicity
 and mitochondrial damage, 71
 and oxidative phosphorylation, 71
 molecular mechanism involving au-
 tooxidation of quinone from 5,6-di-
 hydroxytryptamine and superoxide
 and hydroxyl radicals, 85
 selective target organelles for, 71
- CZ-74 (drug) as inhibitor of serotonin-
 binding protein capacity, 86, 88,
 93
- D**ecarboxylase
 inhibition by RO4-4602, 589
 inhibitors, 437
- Deoxycorticosterone acetate-saline hyper-
 tension in rats, 471

- Desmethylinipramine, 118, 198, 324, 342—343, 388—390, 393, 400, 403, 418, 424, 426, 433, 515, 518, 595—596, 602—603, 605. *See also* in subheads under other main headings, e.g. 5,7-Dihydroxytryptamine—pretreatment of adult rats with desmethylinipramine
- and serotonin-binding protein, 95
- and uptake of various substances in rat brain tissue, 200, 201
- and/or 5,7-dihydroxytryptamine treatment of newborn and their effect on amine uptake *in vitro* in rat brain, 336—337, 336
- antagonizing accumulation of 5,7-dihydroxytryptamine into norepinephrine neurons, 16—17
- as protective agent, 80
- blocking brain norepinephrine transport sites, 107
- blocking uptake of 5,7-dihydroxytryptamine into adrenergic sites, 56
- effect of pretreatment on long-term depletion of brain and spinal cord serotonin and norepinephrine before injection of 5,7-dihydroxytryptamine, 314—315, 316—317
- effect on 5,7-dihydroxytryptamine-induced changes in serotonin and norepinephrine uptake *in vitro* in rat brain cortex, 334, 335
- effect on actions of 5,7-dihydroxytryptamine on newborn rat brain, 165, 165
- effect on retention of brain radioactivity in rats, 108, 110—111, 114—117
- increasing the norepinephrine output evoked, 467
- intraperitoneal injection in rats, 628—629
- pretreatment, 541, 547
- antagonizing brain norepinephrine, 4
- before injection with 5,7-dihydroxytryptamine, 485
- before intracerebroventricular injection of 5,7-dihydroxytryptamine, 472
- in rats, 640—642
- including amines in rat brain cortex, 200, 200
- with 5,7-dihydroxytryptamine intracisternally or intraventricularly, 13
- used to protect norepinephrine neurons from neurotoxic effects of 5,7-dihydroxytryptamine, 440
- Deuterium oxide, 29, 33
- Development of serotonin neurons. *See* Serotonin neuron development
- Developmental plasticity of serotonin neurons. *See* Serotonin neuron development
- 5,6-Diacetoxytryptamine as serotonin neurotoxin, 4, 306
- Dibenamine pretreatment causing degenerative changes in the ultrastructure of cardiac nerves with 5,6-dihydroxytryptamine, 471
- 4,5-Dibenzoyloxyindole synthesis, 25—26, 26
- Dibenzoyloxyindoleacetonitrile synthesis, 29
- 4,5-Dibenzoyloxytryptamine hydrogen oxalate ultraviolet spectra, 31
- 5,6-Dibenzoyloxytryptamine hydrogen oxalate ultraviolet spectra, 31
- 5,7-Dibenzoyloxytryptamine hydrogen oxalate ultraviolet spectra, 31
- β,β -Difluoro-4-chloroamphetamine, 289—291
- β,β -Difluoro-*p*-chloroamphetamine, 152—154
- 5,7-Dihydroxyindoleacetaldehyde role in augmenting 5,7-dihydroxytryptamine toxicity, 54, 55
- 5,6-Dihydroxyindoleacetic acid, 17—18, 54
- binding to rat hypothalamus homogenates, 38—39, 43—45, 52, 53
- identified by thin-layer chromatography, 46
- 5,7-Dihydroxyindoleacetic acid, 54, 118
- binding to rat hypothalamus homogenates, 38—39, 43—45, 52, 53
- identified by thin-layer chromatography, 46
- Dihydroxyindoleamines
- effect on protein synthesis, 99, 100, 103
- Dihydroxymethoxyindoleacetaldehyde synthesis, 27
- 4,5-Dihydroxytryptamine
- impairment of serotonin uptake, 306
- rapid autooxidation preventing application as selective neurotoxic agent, 29
- 4,5-Dihydroxytryptamine hydrochloride synthesis, 28, 28
- 5,6-Dihydroxytryptamine, 17, 107, 178—179, 198, 252, 254—256, 289, 297, 305, 385, 389, 393, 476, 485, 488, 566, 568, 570—573, 638, 665. *See also* in subheads under other main headings, e.g. Avoidance behavior—5,6-dihydroxytryptamine effects

- 5,6-Dihydroxytryptamine—(cont'd)
- α methylation counteracting impairment of serotonin uptake, 307
 - and axonal degeneration after intraventricular injection, 370
 - and behavioral changes, 135—136, 145—146
 - in rats, 139—140
 - and cardiac lesions, 57
 - and cross-linking of protein, 60—61, 69
 - and selective cytotoxicity, 57
 - as tool for morphologic studies of central indoleamine neurons, 322, 323, 324
 - as tool for studying sleep mechanisms in cats, 576—587
 - binding to rat hypothalamus homogenates, 38—39, 43—45, 51
 - biochemical effects when intracisternally injected, 199—200
 - brain lesions, 557—558
 - breakdown at biologic hydrogen ion concentration and 37°C, 53
 - chemical properties, 29, 33
 - chromatography, 60—61, 61, 68—69
 - covalent binding to protein oxygen dependency, 60, 68
 - effect alone and in combination with 5-hydroxytryptophan or 6-hydroxydopamine on brain amines and mounting behavior in male rats, 597, 598, 614
 - effect of intraventricular injection on body weight in male rats, 414, 414
 - brain levels of serotonin, norepinephrine, and dopamine in male rats, 412, 413, 418
 - endocrine organ weights in male rats, 414, 415
 - pituitary growth hormone levels in male rats, 417, 417
 - plasma and pituitary follicle-stimulating hormone in male rats, 417, 418
 - tail length in male rats, 414, 416
 - testicular weight in rats, 414, 416, 419
 - effect of methysergide on cumulative concentration response curve in isolated strips of rabbit aorta, 459, 460
 - effect of *p*-chloroamphetamine on, 260
 - effect on brain biochemistry and behavior in rats, 141, 142
 - effect on capacity of serotonin-binding protein from myenteric plexus, 89—90, 90
 - effect on endogenous norepinephrine, dopamine, serotonin, and 5-hydroxyindoleacetic acid in different parts of brain in cats, 578, 580—581
 - effect on monoamine brain concentrations in rabbits, 247, 249
 - effects of intracerebral injections on monoamine uptake and content, 320, 321
 - effects on the rat central nervous system after intraventricular or intracerebral application and on blood platelets *in vitro*, 595—617
 - enhancing release of melatonin and 5-methoxytryptophol, 388
 - indolic nitrogen of for serotonin neurotoxic effects, 143
 - inhibition of serotonin-binding protein capacity, 88—90, 93
 - injection can increase dopamine turnover, 589
 - intraventricular infusion in fowl, 248
 - irreversible binding to protein, 59, 59, 60, 69
 - maximal velocity, 48-49
 - mechanism of action, 177
 - mechanism of neurotoxicity, 21
 - metabolized by monoamine oxidase in rat hypothalamus homogenates, 47
 - Michaelis constant, 47—48
 - microinjection in rats, 571
 - monoamine oxidase-catalyzed conversion of tryptamine, 41, 44
 - inhibited, 41, 45
 - monoamine oxidase inactivation in brain homogenates, 42, 50
 - in vitro*, 42—43
 - monoamine oxidase inhibited *in vivo*, 43, 51
 - not influencing pituitary stores or circulating growth hormone in prepubertal rats, 391
 - oxygen requirement for binding, 59
 - protein binding after intraventricular injection, 46, 52
 - rats pretreated intraventricularly, 483
 - reaction with molecular oxygen, 19
 - reaction with sulfhydryl groups, 68
 - reactive nucleophiles, 68, 69
 - retarding sexual maturation and massively increasing serum gonadotropins, 399
 - selectivity of action on central monoaminergic neurons, 17—19
 - synthesis, 1

- 5,7-Dihydroxytryptamine—(cont'd)
- turning, contralateral, to lesioned side induced in rats by *d*-lysergic acid diethylamide bitartrate, apomorphine hydrochloride, and lisuride maleate, 605, 608
 - uptake
 - inhibition by α -methyltyramine and serotonin, 62, 64, 71
 - inhibition by cocaine and desmethyl-imipramine, 62, 64, 71
 - temperature-dependent mechanism, 68
 - uptake by atria, 61, 62, 68—69
 - temperature-dependent and irreversible binding, 65, 66, 68—69, 71
 - with 5,7-dihydroxytryptamine and norepinephrine, 62, 64, 68—69, 71
 - vasoconstrictor effect in isolated strips of rabbit aorta, 458—459
 - vasoconstrictor effect in rats and rabbits, 474
- 5,6-Dihydroxytryptamine analogs
- effect on brain biochemistry and behavior in rats, 141, 142
 - neurotoxicity, 160
- 5,6-Dihydroxytryptamine and serotonin
- axonal swelling and accumulation of serotonin fluorescence, 213
 - cf. *p*-chloroamphetamine effects on brain, 645
 - degeneration of serotonergic neurons
 - fluorescent appearances in fowl, 248, 250—251, 252—253
 - in rats and fowl, 242—243
 - reduction of brain levels in rabbits, 254
 - effect on development of neurons, 330
 - effects on synthesis and metabolism, 315
 - impairment of serotonin uptake, 306, 306, 324
 - neuron systems after treatment, 315, 317, 317, 319
 - neurotoxicity 4, 29, 36, 85, 175, 184—185
 - selective degeneration of neurons, 263, 285
 - selective neurotoxic action in brain serotonergic nerves, 480, 489
- 5,6-Dihydroxytryptamine creatinine sulfate $\cdot 2H_2O$ ultraviolet spectra, 29, 30, 33
- [1- ^{14}C]-5,6-Dihydroxytryptamine
- accumulation and retention in tissue slices, 308, 310—311, 310, 311
 - brain regional patterns of radioactivity after intraventricular injection, 108, 109, 114—117
 - in rats treated with benzotropine, 110, 110
 - metabolism in rat brain *in vivo*, 17—18
 - radioactivity in hypothalamus, pons-medulla oblongata, and spinal cord after intraventricular injection, 5, 6
 - radioactivity in rat perchloric acid-homogenized central nervous system, 7, 9, 10, 11
 - radioactivity in rat urine after intraventricular injection, 5, 9, 19
- 5,7-Dihydroxytryptamine, 107, 118, 178—179, 198, 254, 289, 297, 328, 343, 385, 388, 390, 400, 456, 476—477, 479, 485, 488, 530—531, 566, 568, 571, 573, 664. *See also* in sub-heads under other main headings, e.g. Brain mitochondria—interaction of 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine in rats
- α -methylation counteracting impairment of serotonin uptake, 307
 - and forced extinction with intrabrain stem injections, 362—363, 365—366
 - and hyperactivity in rats, 478
 - and inhibition of monoamine oxidase, 58
 - and metabolites of neurotransmitter compounds, 173
 - and selective cytotoxicity, 57
 - and uptake of various substances by rat brain tissue, 200, 201
 - appearance of rat brain dorsal raphe (B7) after intraventricular injection, 296, 298—299
 - as tool for morphologic studies of central indoleamine neurons, 322, 323, 324
 - better tool than 5,6-dihydroxytryptamine for mapping central serotonin neurons, 346
 - binding sites in brain, 118
 - binding sites in lumbar spinal cord, 118
 - binding to mitochondria, 67
 - binding to rat hypothalamus homogenates, 38—39, 43—45, 51
 - biochemical effects when intracisternally injected, 199—200
 - blood-brain barrier for, 331

5,7-Dihydroxytryptamine—(cont'd)

brain content of 5-hydroxyindoleacetic acid, homovanillic acid, and 3-methoxyphenylglycol sulfate in male rats injected in the right medial forebrain bundle after pretreatment with desmethylimipramine, 605, 606, 612

brain content of serotonin, dopamine, and norepinephrine after injection in the right medial forebrain bundle of rats pretreated intraperitoneally with desmethylimipramine or maprotiline, 603, 604, 605, 612

brain lesions, 557—558

breakdown at biologic hydrogen ion concentration and 37°C, 53

cause of considerable degeneration of norepinephrine neurons and dopamine systems, 346

changes in brain monoamines and their metabolites induced in rats pretreated with harmaline or Lu 10-171, 597, 600, 601, 613

changes in systolic blood pressure, pulse rate, and body weight after intracerebroventricular injection in spontaneously hypertensive rats, 472, 473

chemical properties, 29, 33

chosen over 5,6-dihydroxytryptamine because of lower toxicity, 438

chromatography, 60, 61, 68—69

continuous infusion into aortic cannula of an isolated rabbit heart, 465, 465

correlation between decrease in cortical serotonin turnover and the increase in striatal dopamine turnover in rats injected unilaterally into median raphe nucleus or substantia nigra, 526—527, 527

cysteinyl-tyrosyl bridge, 70

discrepancy between effects and those of a raphe lesion, 445

dopamine content after treatment of forebrain in male rats, 426, 427

duration of effects on brain monoamine oxidase content, 161—162, 162, 164—165

effect of 1-phenyl-3-(2-thiazolyl)-2-thiourea, ethanol, and nialamide on the neurodegenerative action, 78, 79, 81

effect of centrally acting drugs on brain monoamine oxidase content, 162—163, 163, 165

effect of intracisternal injection on amines in rat cerebral cortex, 200, 200

effect of *p*-chloroamphetamine on, 260

effect of various doses administered on brain monoamines in newborn rats, 163—164, 164

effect on dopamine uptake, 528

effect on locomotor activity when neonatally injected into rats, 165—166, 166

effect on mounting behavior of male and female rats pretreated with desmethylimipramine, harmaline, or Lu 10-171, 602, 602, 614

effect on norepinephrine output, heart rate, and positive chronotropic effect of exogenous norepinephrine in isolated rabbit hearts, 465, 466, 469

effect on peripheral norepinephrine neurons, 57

effect on proestrous surges of luteinizing hormone and prolactin in female rats, 403, 404

effect on serum levels of luteinizing hormone, prolactin, and growth hormone in rats, 409

effect on tegmentum, 188

effect on tyrosine hydroxylase activity, 528

effect when injected

into median raphe nucleus in rats on serotonin and 5-hydroxyindoleacetic acid levels and serotonin and norepinephrine uptake, 525, 525

into the medial forebrain bundle on the methiothepin-induced increase of monoamine metabolites in male rats, 605, 607, 612

intraventricularly on increase of 5-hydroxyindoleacetic acid and homovanillic acid induced by methiopropin in rats, 597, 600

effects of intracerebral injections on monoamine uptake and content, 320, 321

effects of intracerebroventricular injection on systolic blood pressure, pulse rate, and body weight of conscious spontaneously hypertensive rats, 472, 473

effects of intraventricular injection on rat forebrain norepinephrine concentration, 439, 439

5,7-Dihydroxytryptamine—(cont'd)

- effects of intraventricular injection on
 - rat forebrain norepinephrine, dopamine, and serotonin and brain stem serotonin, 439, 440
- effects of monoamine oxidase inhibitors on, 162, 162
- effects on serum values in rats on the afternoon of estrus, 402, 404
- effects on suckling-induced prolactin rise in female rats, 405, 405
- effects on the rat central nervous system after intraventricular or intracerebral application and on blood platelets *in vitro*, 595—617
- efflux from atria, 65, 66, 71
- electroshock seizure threshold in rats, 444, 447
- formation of hydrogen peroxide from oxidative deamination, catalyzed by monoamine oxidase, 74, 75
- given to produce brain lesions in rats, 364—366
- impairment of norepinephrine uptake, 307
- in combination with a catecholamine uptake blocking agent, 497—498
- influence on effect of electrical stimulation of postganglionic sympathetic nerves of an isolated rabbit heart, 465, 467, 469—470
- inhibition of serotonin-binding protein capacity, 88—89, 93
- inhibition of uptake, 84
- injection can increase dopamine turnover, 589
- intracisternal injection in rats, 628
- irreversible binding to protein, 59, 59, 60, 69
- keto-enol tautomeric forms, 29, 32
- maximal velocity, 48—49
- measures of body weight and food and water intake after intracisternal injection in rats, 632, 632
- mechanism of action, 177
- metabolized by monoamine oxidase in rat hypothalamus homogenates, 47
- Michaelis constant, 47
- microinjection in rats, 571
- monoamine analyses
 - after anticonvulsant testing in treated rats, 450, 451
 - in rats, 444, 445, 447
- monoamine oxidase and, 69
- monoamine oxidase-catalyzed conversion of tryptamine, 41, 46
- inhibited, 41, 47

monoamine oxidase inactivation
in brain homogenates, 43, 50
in vitro, 42—43

in vivo, 43, 51

monoamines in rat central nervous system after given alone or to animals pretreated with uptake inhibitors, 597, 599, 612

norepinephrine content of forebrain and brain stem in treated male rats, 426, 426

o-quinone of. *See o*-Quinone of 5,7-dihydroxytryptamine

oscillatory luteinizing hormone pattern in ovariectomized rats after treatment, 427, 431

p-quinoneimine of. *See p*-Quinoneimine of 5,7-dihydroxytryptamine
possible enhancement of toxicity of metabolism, 54—55

pretreatment of adult rats with desmethylimipramine, 524

pretreatment with, and locomotor activity, 173—174

protein binding after intraventricular injection, 46, 52

rats pretreated intraventricularly with, 483

reaction product with cysteine and tyrosine residues, 70—71, 70

reaction with molecular oxygen, 19

reactive aldehyde, 70, 70

reducing luteinizing hormone levels in rats treated, 432

response of rats to maximal electroshock, 443, 444

restored circhoral luteinizing hormone pattern in ovariectomized rats after treatment, 427, 431

selectivity of section on central monoaminergic neurons, 17—18

serum luteinizing hormone and prolactin levels in treated proestrous rats, 430, 432

serum luteinizing hormone, prolactin, and monoamine levels in hypothalamus of treated ovariectomized rats, 427, 428

serum prolactin, luteinizing hormone, and follicle-stimulating hormone levels

in ether-stressed treated rats, 426, 430

in mildly stressed male rats, 425, 425

sex-related differences in response to, 174

specificity, 334, 336—337, 528

subcellular distribution, 67, 67, 71

- 5,7-Dihydroxytryptamine—(cont'd)
 supersensitivity produced by, 260
 toxicity to norepinephrine neurons
 overcome by pretreatment of animals with protriptyline, 438
 tritium overflow in brain slices of treated rats, 334, 335, 336
 tyrosyl derivative, 70, 70
 uptake
 dose-dependent loss of with 6-hydroxydopamine or 5,7-dihydroxytryptamine, 71
 inhibition by α -methyltyramine and serotonin, 62, 64
 inhibition by cocaine and desmethyl-imipramine, 62, 64, 71
 pretreatment with 6-hydroxydopamine, 5,7-dihydroxytryptamine, or 5,6-dihydroxytryptamine, 62, 64
 uptake and accumulation in norepinephrine neurons, 21
 uptake by atria, 61, 63, 71
 plus 5,6-dihydroxytryptamine and norepinephrine, 62, 64, 68—69, 71
 uptake by brain, 176
 vasoconstrictor effect in
 isolated strips of rabbit aorta, 458—459
 rats and rabbits, 474
5,7-Dihydroxytryptamine and serotonin, 73
 and brain concentration, 171—172
 and regeneration within central pathways, 346
 cf. *p*-chloroamphetamine effects on brain, 645
 content in rat brain after treatment, 426, 429
 effect of neonatal administration to rats on *in vitro* serotonin uptake, 331, 332
 with 6-hydroxytryptamine and desmethylimipramine on fluorescence histochemical demonstration of nerve terminals, 332, 333
 effect of pathway lesions in rat mid-brain on
 acquisition of one-way avoidance response, 352, 352
 forced extinction of one-way avoidance response, 352, 353
 retention of one-way avoidance response, 352, 353
 effect on central neurons, 3—4, 57
 effect on development of neurons, 330
 effect when administered to rats on *in vitro* serotonin uptake, 330—331, 331
 impairment of serotonin uptake, 306, 324
 metabolism and neurotoxicity, 20—21
 neurotoxicity, 4—5, 21, 29, 36, 85, 175, 186, 296, 480, 489
 reducing brain serotonin and norepinephrine, 166
 reducing brain serotonin content after pretreatment with desmethylimipramine, 434
 reducing serotonin, 167—168
 selective degeneration of serotonergic neurons, 263, 285
 specificity in reducing serotonin content, 432—433
5,7-Dihydroxytryptamine creatinine sulfate
 changes in ultraviolet absorption with hydrogen ion concentration, 29, 32
 ultraviolet spectra, 29, 30, 33
 after reaction with oxygen, 33, 33
[¹⁴C]-5,7-Dihydroxytryptamine
 accumulation and retention in tissue slices, 308, 310—311, 310, 311
 affinity for brain serotonin and norepinephrine uptake sites, 16—17
 brain regional patterns of radioactivity after intraventricular injection, 108, 109, 114—117
 in rats treated with desmethylimipramine, 111, 113
 in rats treated with pargyline, 110—111, 112
 in rats treated with 6-hydroxydopamine combined with nialamide, 111, 113
 comparison of intraventricular and intracisternal routes of administration, 12—16
 effect of injection route on regional retention of radioactivity, 12, 13
 increase in fractions from caudal spinal cord, 117—118
 radioactivity in hypothalamus, pons-medulla oblongata, and spinal cord after intraventricular injection, 5, 7, 8
 radioactivity in rat perchloric acid-homogenized central nervous system, 7, 9, 10, 11
 radioactivity in rat urine after intraventricular injection, 5, 9, 19
6,7-Dihydroxytryptamine
 biochemical effects when intracisternally injected, 199
 impairment of norepinephrine uptake, 307

- 6,7-Dihydroxytryptamine—(cont'd)
 impairment of serotonin uptake, 306
o-Dihydroxytryptamines and serotonin, 25, 33
- 3,4-Dimethoxyamphetamine, 126
 as metabolite of *p*-chloroamphetamine, 176
 in brain, 120, 124—125
 as psychotoxic agent, 124
- 5,6-Dimethoxytryptamine
 biochemical and behavioral effects in the rat, 140—141
- 6,7-Dimethyl-5,6,7,8-tetrahydropterine, 583
- N,N*-Dimethyltryptamine 487
- o,w*-Dinitrostyrenes, 25—26
- Dithiothreitol
 antagonizing toxic action of 5,6-dihydroxytryptamine on monoamine oxidase, 53
 preventing oxidation of 5,6-dihydroxytryptamine but not 5,7-dihydroxytryptamine, 54
- Dopa, 525
 accumulation, 221
 determination in brain, 223—224
 rat brain concentration after fenfluramine administration, 232—233, 237
- L-Dopa, 389—390, 479, 613, 664
 ineffective in producing myoclonic syndrome in rats, 551
 occasional hypersexuality seen in patients during therapy of parkinsonism, 613
- Dopa decarboxylase, 583-585
- Dopamine, 118, 252, 388—391, 412, 414, 498, 510, 519—520, 530—531, 576, 578, 602, 612—613, 616.
See also in subheads under other main headings, e.g. 5,7-Dihydroxytryptamine—effect on dopamine uptake
 analyzed in rat forebrain, 439—440
 brain and spinal cord levels after treatment with 5,7-dihydroxytryptamine or *p*-chlorophenylalanine in rats, 498, 499, 503
 effect of 5,7-dihydroxytryptamine-induced lesions of serotonin pathways of midbrain on level
 in front of the lesion in rats, 355, 356
 within cortex of rats, 354, 354, 356
 in brain, 423, 432, 540, 547
 after intraventricular injection of 5,6-dihydroxytryptamine, 3
 cortex of rats, 365
 of female rats, 621
 of rats, 631
 telencephalon and diencephalon of rats, 349
 in unilaterally lesioned rats, amphetamine thought to induce ipsilateral turning by releasing, 524
 influence of 5,7-dihydroxytryptamine, α -methyl-5,7-dihydroxytryptamine, and desmethylinipramine on forebrain, 14—16, 15
 long-term depletion in brain, 20
 mean concentrations after administration of 5,7-dihydroxytryptamine into rats, 590—591, 592
 measured by radioenzymatic catechol *O*-methyltransferase method, 424
 role in luteinizing hormone release, 388
 uptake by synaptosomes, 92
- Dopamine β -hydroxylase, 182—184, 583—587
- Dopamine denervation hypersensitivity, 406
- Dopamine neurons, 107, 114—116, 342—343, 527, 530, 540
 in rat brain, 336
 regeneration after 5,7-dihydroxytryptamine treatment, 385
- Dopamine receptor agonists, 595, 603, 605, 612—616. *See also* Apomorphine, *d*-Lysergic acid diethylamide; Ergocornine; Ergometrine; Piribedil
- Dopamine releasers. *See d*-Methamphetamine; Methylphenidate
- Dopaminergic-binding protein, 94
- Drinking, 484—485
 altered by 5-hydroxytryptophan administration in rats, 556
 changes in monkeys and rats, 566, 568
 deficits when 5,6-dihydroxytryptamine microinjected in monkeys and rats, 570—571
 hypodipsia, 484—485. *See also p*-Chlorophenylalanine and serotonin hypothalamic actions of serotonin neurotoxins, 573
 in rats, 628—629
 mean daily water intake for rats after serotonin injection and 5,6-dihydroxytryptamine, 566, 567
 regulated in rats, 628

Drugs, centrally acting

effect on actions of 5,7-dihydroxytryptamine in adult rats, 161—163

Drugs, intraventricular vs. intracisternal injections producing different effects, 171

Eating. *See* Feeding

β -Endorphin effect on growth hormone release in rats, 422

met-Enkephalin effect on growth hormone release in rats, 422

Enzymes. *See also* as main headings or in subheads under other main headings: Acetylcholinesterase; Adenyl cyclase; Aldehyde dehydrogenase; Brain—enzymatic activity; Catalase; Catechol *O*-methyltransferase; Choline acetylase; Choline acetyltransferase; Decarboxylase; Dopa decarboxylase; Dopamine β -hydroxylase; Hydroxyindole *O*-methyltransferase; Hydroxylases; Monoamine oxidase; Oxidase; Peroxidase, horseradish; Phenylalanine hydroxylase; Superoxide dismutase; Tryptophan hydroxylase; Tyrosine hydroxylase

activity in the locus ceruleus after intracisternal injection of 5,6-dihydroxytryptamine, 583, 584

inhibitors. *See* Monoamine oxidase inhibitors; RO4-4602

Ergocornine, 605

Ergometrine, 605

Estradiol benzoate, 622—624

Estrous cycles in rats, 430, 433

Ethanol as hydroxyl radical scavenger, 82, 84

Ethylene-generating system for measuring flux of hydroxyl radicals, 75

Ethylene production by catalase, superoxide dismutase, and hydroxyl radical scavengers suppressed, 76—77, 76, 80—81

Feeding, 484—485. *See also* Anorexia; Drinking; Hyperphagia

altered by 5-hydroxytryptophan administration in rats, 556

amino acids in rats, 641—642

changes in monkeys and rats, 566—568
deficits when 5,6-dihydroxytryptamine microinjected in monkeys and rats, 570—571

finickiness in rats, 627—628, 630, 634, 642

high-fat diet, 628, 630

hypothalamic actions of serotonin neurotoxins, 573

intake after

intraventricular injection of *p*-chlorophenylalanine methyl ester in rats, 590, 591

p-chlorophenylalanine- and sham-injected rats, 593, 593

serotonin and 5,6-dihydroxytryptamine injection in rats, 566, 567

intake in rats, 628—629, 638, 640

obesity, 484, 490

suppression by serotonin system, 594

Fenfluramine, 150, 178, 289—291, 296—297, 300, 302—304, 488—490, 498. *See also* in subheads under other main headings, e.g. 5-Hydroxyindoleacetic acid—brain concentration—after fenfluramine administration in newborn and adult rats

administration, 123
and newborn rats, 239
and tryptophan 5-hydroxylase activity, 126

brains in rats injected later with fluoxetine, 229, 233

can induce anorexia, 478

determination in plasma and brain by gas chromatography, 224

mass spectrometry, 224—225

effect in newborn animals, 172

effect on brain B9 region in rats, 293, 295, 296

hyperthermic effects, 255—256

influence of administration route on brain levels, 120, 120

main site of action, 238

metabolism, 126

metabolite accumulation after brain injection, 120, 121

method to differentiate from norfenfluramine, 241

neurotoxicity, 125, 127, 259, 480, 482, 484

plasma and brain concentration in rats, 225—226, 227, 228

powerful anorectic agent, 556

subcellular distribution of metabolites after brain injection, 121, 122

suppression of female mating, 621

time course for decrease in serotonin and 5-hydroxyindoleacetic acid in rat brain produced by, 225, 226

Fenfluramine—(cont'd)

used for regulation of body weight in human beings, 485

Fenfluramine and serotonin

and reduction of brain serotonin and 5-hydroxyindoleacetic acid, 119
and serotonin-binding protein capacity, 91

effect of acute and chronic injection on brain serotonin content in rats, 296, 296

effect on brain serotonin content when fenfluramine neonatally administered in rats, 163—164, 164

effect on content in rat brain regions, 292, 295

effect on serotonergic terminal processes, 222

possible serotonin deficiency, 1

relation of concentration in brain to serotonin depletion, 222

serotonin releasing, 621

p-Fluoroamphetamine, 150, 154, 289—291

Fluoxetine, 172, 289—290, 476, 515, 519, 649. *See also* in subheads under other main headings, e.g. *p*-Chloroamphetamine—interaction with fluoxetine in mice

ability to reverse action of fenfluramine, 238

and brain uptake and metabolism of amphetamines, 121

and protein synthesis, 105—106

and serotonin-binding protein, 95

as inhibitor of serotonin-binding protein capacity, 92

blocking of anorectic effects of fenfluramine, 241

effects on *p*-chloroamphetamine, 158—159

effects on serum prolactin and brain and hypothalamic serotonin and norepinephrine concentrations in female rats, 406, 407

high dosage with serotonin producing myoclonus, 207

inducing analgesia, 487

inhibition of mixed-function oxidase activity, 215

metabolism in brain, 124

potentiating action of 5-hydroxytryptophan 389, 392

selectivity in rat brain, 229, 233

significantly blocking all aspects of the *p*-chloroamphetamine-induced myoclonic syndrome in rats, 518

significantly decreasing serotonin re-uptake, 503

stimulant effects of *p*-chloroamphetamine blocked in pretreated animals, 482

termination of norfenfluramine serotonin-reducing action, 236

termination of serotonin-lowering action of fenfluramine, 226—227, 229

unavailable to protect serotonin fibers from 5,6-dihydroxytryptamine, 613

Follicle-stimulating hormone, 387—389, 412, 419—420, 434

determined by radioimmunoassay, 424

inhibitory effect of serotonin on release, 433

Food. *See* Feeding

Gastrointestinal system

autopsies in rats, 635—636

motility in rats, 640

pathology in rats, 631, 640

Glutathione

antagonized toxic action of 5,6-dihydroxytryptamine on monoamine oxidase, 53

prevention of oxidation of 5,6-dihydroxytryptamine but not 5,7-dihydroxytryptamine, 54

Glutathione, reduced

effect on brain serotonin, 121, 123

Gonadotropin release elevated by progesterone, 624

Gramine synthesis of indole derivatives via, 27, 27

Growth hormone, 390—391, 399—400, 412, 419—420

in rats, 630, 638, 641

plasma levels reduced by stress in rats, 422

role of serotonin in regulating in primates, 391

Guanosine triphosphate as inhibitor of serotonin-binding protein capacity, 91

Habituation to novel stimuli by rats, 486—487

Halogenated amphetamines. *See also* *p*-Bromoamphetamine; *p*-Chloroamphetamine; β , β -Difluoro-4-chloroamphetamine; Fenfluramine; *p*-Fluoroamphetamine

effect blocked by fluoxetine, 292

- Halogenated amphetamines—(cont'd)
 effect of chronic treatment, 292, 296
 effect on brain serotonin, 291
 neurotoxicity, 289—300
- Haloperidol, 515, 518—519
 blocking response to amphetamine and apomorphine re contralateral rotation in rats, 526
- Harmaline, 596, 602, 613
- Heart rate
 increase induced by
 bolus injections of 5,7-dihydroxytryptamine, 468, 468
 tryptamine derivatives and some other amines on right atrial strips of guinea pigs, 462, 463
 tryptamine derivatives on right atrial strips of guinea pigs, 461—462, 461
 isolated hearts of rabbits, 462, 465
 positive chronotropic effect of 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine, 461—462
 spontaneously beating right atria of guinea pigs, 461
- Hippocampus
 depletion of serotonin by *p*-chloroamphetamine, 196—197
 loss of the serotonin innervating, 453
 perfusion with serotonin increased seizure activity in rats, 437
- Hippurates and enzymatic synthesis in rat brain homogenates, 122, 123
- Histamine, 462
- Homovanillic acid, 118, 173, 596—597, 605, 612—613, 615—616
- Hormones. *See also* as main headings or in subheads under other main headings: Adrenocorticotrophic hormone; Estrogen; Follicle-stimulating hormone; Gonadotropins; Growth hormone; Luteinizing hormone; Melanocyte-stimulating hormone; Progesterone; Prolactin; Thyroid-releasing hormone; Thyroid-stimulating hormone
 used as terminal neuroendocrine measures, 638, 639, 641
- 5-Hydroxy-7-chlorotryptamine, 175
- 5-Hydroxy-6-methoxyindoleacetic acid, 17
- 4-Hydroxy-5-methoxytryptamine
 rapid autooxidation preventing application as selective neurotoxic agent, 29
- 4-Hydroxy-5-methoxytryptamine hydrochloride ultraviolet spectra, 29, 30, 33
- 5-Hydroxy-6-methoxytryptamine, 18
 and alteration of dopaminergic neurotransmission, 146
 biochemical and behavioral effects in rats, 140
- 3-Hydroxybenzylhydrazine hydrochloride, 223, 225, 232—235, 237
- 6-Hydroxydopamine, 53, 76—78, 107, 114—117, 254—255, 289, 297, 328, 339, 342, 362, 406, 436, 478, 530, 566, 568, 570, 594, 631, 649, 664. *See also* in subheads under other main headings, e.g. 5,6-Dihydroxytryptamine—effect alone and in combination with 5-hydroxytryptophan or 6-hydroxydopamine on brain amines and mounting behavior in male rats
- 1,4-*p*-quinone derivative of, 68
 and neuroblastoma cells, 68
 and regeneration in catecholamine-containing neurons, 370
 autooxidation, 57
 autooxidative and enzymatic formation from dopamine, 135
 cytotoxicity, 57
 degeneration of central catecholaminergic fibers by intraventricular and intracisternal injection, 19
 effect of reducing agents on, 68
 effect of polysomal profiles, 102, 103
 effect on protein synthesis, 98—99, 99, 100, 101—103, 101
 for lesioning central catecholamine neurons, 505
 for lesioning rats, 605, 609, 614
 formation of 2,5-dicysteinyl derivative, 68
 formation of hydrogen peroxide from spontaneous reaction with oxygen, 74, 75
 inhibition of uptake, 84
 introduction, 1
 lesions, 526—527
 long-lasting depletion of norepinephrine in peripheral organs, 36
 mechanism of action, 80
 neurotoxicity, 160, 184—185
 paraquinone of, 57
 paraquinone reaction with free sulfhydryl group, 68
 quinoidal products, 80—82
 shown after intracisternal injection, 342
 uptake by atria
 5,7-dihydroxytryptamine, 5,6-dihydroxytryptamine, and norepinephrine, 62, 64, 68—69, 71

5-Hydroxyindole, 390

Hydroxyindole derivatives and serotonin-binding protein, 95

5,6-Hydroxyindoleacetaldehyde, 18

5-Hydroxyindoleacetic acid, 199, 208, 211, 213, 217, 239, 525, 530—531, 533, 576, 578—579, 596—597, 600, 605, 612—613, 616, 621. *See also* *p*-Chloroamphetamine—influence on brain concentration of serotonin and 5-hydroxyindoleacetic acid

brain concentration, 152

after fenfluramine administration in newborn and adult rats, 231, 236

after norfenfluramine administration in rats, 229, 234

after *p*-chloroamphetamine intraperitoneally injected in rats, 515, 517

after treatment with fluoxetine in rats, 227, 228, 229

determination, 222—223

effect of 5,6-dimethoxytryptamine on, 140—141

formation from tryptophan in different central nervous system regions of rats, 315, 318

in brain of rats, 519—520, 631, 636, 638

in central nervous system, 4

increase caused by 5,6-dihydroxytryptamine and 3-(β -aminoethyl)-5,6-dihydroxybenzo[*b*]thiophene, 139

increase or decrease caused by 5-hydroxy-6-methoxytryptamine, 140

permanence of recovery in brain induced by fluoxetine in rats, 227, 231

probenecid-induced accumulation in cerebrospinal fluid and brain, 300, 304

reduced in brain by *p*-chloroamphetamine in rats, 645

spectrofluorometric assay from brain, 400

substantially blocking hyperphagia and obesity following medial hypothalamic lesion in rats, 628

[³H]-5-Hydroxyindoleacetic acid

metabolism from [³H]-tryptophan, 373, 374—375, 376

Hydroxyl radicals

effect of scavenger on the neurodegenerative action of 6-hydroxydopamine and 6-aminodopamine, 77, 78, 80—81

from superoxide and hydrogen peroxide, 75, 76—77, 80

role of 6-hydroxydopamine in neurotoxicity, 74

scavengers. *See* Ethanol; 1-Phenyl-3-(2-thiazolyl)-2-thiourea

Hydroxylases

brain and spinal cord activities of tryptophan, tyrosine, and dopamine β -hydroxylases, 184, 184

effect of 5,6-dihydroxytryptamine on brain and spinal cord activities of tyrosine and dopamine β -hydroxylases, 185, 185

Hydroxymethoxyindoleacetaldehyde synthesis, 27

2-[β -(4-Hydroxyphenyl)ethylamino-methyl]tetralone, 457—458

antagonism of methysergide and toward the contractile response to vasoconstrictor amines in aorta of rabbits 360, 460

cf. methysergide and on cumulative concentration-response curve of 5,6-dihydroxytryptamine in aorta of rabbits, 460, 461

6-Hydroxytryptamine

as inhibitor of serotonin-binding protein capacity, 86, 88, 93

neurotoxicity on catecholamine cell bodies, 300

5-Hydroxytryptophan, 254-256, 260, 284,

366, 389-390, 392-394, 437, 444, 481, 483, 485, 487, 525, 590, 602, 613, 615—616, 621, 627, 664. *See also* in subheads under other main headings, e.g. *p*-Chlorophenylalanine—mounting behavior in male, female, castrated, and ovariectomized rats alone or in combination with 5-hydroxytryptophan or haloperidol

able to block preovulatory luteinizing hormone discharge in intact rats, 423

administered intraperitoneally to rats pretreated with intracranial injections of 5,7-dihydroxytryptamine, 510, 519

administration intraperitoneally elevating brain serotonin, 388

and brain serotonin, 484

and increase in circulating growth hormone level, 391

and reduction of tryptophan 5-hydroxylase, 119

blocking of ovulation, 399

- 5-Hydroxytryptophan—(cont'd)
- brain concentration after fenfluramine administration in rats, 232—233, 237
 - causing release of melanocyte-stimulating hormone after administration in frogs, 394
 - determination in brain, 223—224
 - effect on prolactin release in rats pretreated with
 - 5,7-dihydroxytryptamine, 408, 408
 - p*-chloroamphetamine, 408—409, 408
 - effects on serum prolactin, brain and hypothalamic serotonin, and brain and hypothalamic norepinephrine concentrations in female rats, 406, 407
 - in brain serotonin biosynthesis, 483
 - increasing release of corticosteroids after total interruption of neural afferents to hypothalamus, 393
 - inducing prolactin rise in both *p*-chloroamphetamine- and 5,7-dihydroxytryptamine-treated animals, 410
 - injected rats, earlier injected with desmethylimipramine and intracranial 5,7-dihydroxytryptamine, 510—511, 512
 - restoring cyclicity of luteinizing hormone, 389
 - supersensitivity to, 239
- 5-Hydroxytryptophan-induced neurologic syndrome
- antiserotonin agents, 203
 - behavior after administration of desmethylimipramine plus 5,7-dihydroxytryptamine, 203, 205
 - denervation supersensitivity, 205
 - myoclonus, 204—207
 - myoclonus after intracisternal injection of 5,7-dihydroxytryptamine, 201—203, 202
 - myoclonus effect of drug treatment in 5,7-dihydroxytryptamine- plus desmethylimipramine-lesioned rats, 204, 205
 - pharmacologic studies, 203
 - postsynaptic serotonin receptor mechanisms, 205
 - presynaptic mechanisms, 205
- 6-Hydroxytryptophan, 285
- Hyperphagia. *See also p*-Chlorophenylalanine; 5-Hydroxyindoleacetic acid
- 5-hydroxytryptophan reversed *p*-chlorophenylalanine-induced in rats, 590, 591
 - and obesity, 485
 - central injection of 5,7-dihydroxytryptamine to desmethylimipramine-pretreated adult female rats did not induce, 638
 - failure of 5,7-dihydroxytryptamine to produce, 590
 - in rats, 484, 642
 - induced by systemic injection of gold thioglucose in mice, 627
- Hypertension. *See also* Deoxycorticosterone acetate-saline hypertension in rats
- regulation by central serotonergic neurons in rats and rabbits, 471
 - regulation in rats and rabbits, 474
- Hyperthermia, 251—252, 254—256, 558.
- See also d*-Amphetamine; Apomorphine; Chlorpromazine and prevention of lethal hyperthermia; Fenfluramine; Pimozide; Sleeping and waking
 - and pretreatment effect of *p*-chlorophenylalanine or 5,6-dihydroxytryptamine in rabbits, 245—247
 - induced by
 - 5-hydroxytryptophan plus phenylethylhydrazine in rabbits, 246, 248
 - apomorphine in rabbits, 246, 246, 255—256
 - bacterial pyrogen in rabbits, 246, 247
 - d*-amphetamine in rabbits, 245—246, 245, 255—256
 - fenfluramine and serotonin in control and 5,6-dihydroxytryptamine-treated fowl, 251, 251
 - fenfluramine in rabbits, 247, 250
 - injection of 5,7-dihydroxytryptamine in rats, 665
 - injection of serotonin in cats, 242
- Hypodipsia. *See p*-Chlorophenylalanine and serotonin; Drinking
- Hypothalamohypophyseal portal capillaries, 387
- Hypothalamus, 393—395
- action of 5,6-dihydroxytryptamine on in monkeys and rats, 568, 570—572
 - dopamine levels, 429
 - fall in serotonin level, 392
 - lesion in rats, 572
 - mesencephalic norepinephrine fibers play key role in stimulating preovulatory luteinizing hormone surge, 423

- Hypothalamus—(cont'd)
 monoaminergic innervation, 423
 norepinephrine levels, 429, 434
 serotonin cell bodies, 436
 serotonin content after 5,7-dihydroxytryptamine administration, 429
 synaptosomes in rats, 128
- Hypothermia. *See also* Apomorphine
 fatal in monkeys, 563—564
 induced by injection of norepinephrine in cats, 242
- I**ndole derivatives
 inhibition of serotonin-binding protein, 86
- Indoleamines, 129—132, 470, 472
 histofluorescence, 244
- Indolectomy, chemical, 387—395
 5,6-*o*-Indolquinone, 36
- Iprindole administration, 124
- Iprindole and brain uptake and metabolism of amphetamines, 121
- Iproniazid, 470
 uptake by atria of 5,7-dihydroxytryptamine, 5,6-dihydroxytryptamine, and norepinephrine, 62, 64
- Isoleucine, 642
- Isoprenaline, 462
- K**ainic acid, 530
- L**ecucine, 642
- Lineweaver-Burk representations, 40—41, 41, 43, 44, 46, 47, 48
- Lisuride maleate, 596, 605
 given intraperitoneally and tested for inducing contralateral turning in rats, 605, 608, 614—616
- Locomotor activity, 480—482
 effects of serotonin neurotoxic drugs on, 481—482
 hyperactivity vs. hypoactivity, 481
 hyperactivity, 482
 hypoactivity, 482
 in rats, 664
- Locus ceruleus
 and unilateral rotational behavior when lesioned, 589
 in brain of cats, 582—587
- Lordosis mediation by estrogen in female rats, 623—624
- Lu 10-171, 596, 602, 613
 preventing both serotonin depletion and the occurrence of mounting behavior in rats, 614
 preventing destruction of serotonergic system, 56
- Luteinizing hormone, 362—363, 387—389, 400, 423, 432—434
 change of rhythm after ovariectomy plus 5,7-dihydroxytryptamine, 436
 determined by radioimmunoassay, 424
 inhibitory effects of serotonin infusion into cerebrospinal fluid, 399
 surges induced by estrogen administration blocked by *p*-chlorophenylalanine injection in ovariectomized rats, 399
- d*-Lysergic acid diethylamide, 203, 204, 207, 260, 349, 363, 487—488, 498, 596, 605, 614—616, 664
 as inhibitor of serotonin-binding protein capacity, 91
 binding *in vitro* in brain of rats, 337, 338, 342—343
 blocked myoclonic syndrome in rats, 511
- d*-Lysergic acid diethylamide-induced behavioral syndrome in rats, 406
- [³H]-*d*-Lysergic acid diethylamide
 binding in rat cerebral cortex, 351, 358—360, 358, 359, 360, 361, 362
 after serotonin denervation of forebrain, 364—366
- M**aprotiline, 596, 603, 612—613
 Mating behavior. *See* Sexual behavior
- Melanocyte-stimulating hormone, 394
- Melatonin
 in rats, 631, 638
 inhibitory influence on pituitary gonadotropin secretion, 388
- Metaraminol, 597
- d*-Methamphetamine, 302, 605, 615
- Methergoline, 515, 518—519
 as blocker of serotonin receptors, 392
- Methimazole structure, 77, 77, 80—81
- Methiopin, 389, 515, 518—519
 as blocker of cerebral serotonin, dopamine, and norepinephrine receptors, 597, 605, 612
- 5-Methoxy-*N,N*-dimethyltryptamine, 254, 498
 producing myoclonic syndrome in rats, 511
- 5-Methoxy-6-hydroxyindoleacetic acid, 17
- 3-Methoxy-4-hydroxyphenylethyleneglycol, 173
- 3-Methoxy-4-hydroxyphenylethyleneglycol sulfate, 582, 597, 605, 612—613, 616

- 5-Methoxy-6-hydroxytryptamine, 17
 biochemical and behavioral effects in rats, 140
- 6-Methoxy-5-hydroxytryptamine, 17
- 5-Methoxytryptamine, 538
- 5-Methoxytryptophol inhibitory influence on pituitary gonadotropin secretion, 388
- α -Methyl-5,6-dihydroxytryptamine, 69
- α -Methyl-5,7-dihydroxytryptamine, 116
 and cytotoxicity, 58
 as serotonin neurotoxin, 4—5
 cytotoxicity, lack of effect with, 69
 intraventricular cf. intracisternal routes of administration, 12—16, 14, 15
 molar neurotoxicity, 20—21
 toxic effects on norepinephrine- and serotonin-containing brain axons, 11
- N-Methyl-5,6-dihydroxytryptamine impairment of norepinephrine uptake, 307
- N-Methyl-5,7-dihydroxytryptamine impairment of norepinephrine uptake, 307
- α -Methyl-5-hydroxytryptamine
 as serotonergic false neurotransmitter, 194
 measurement by chromatography, 191, 191
 use to deplete serotonin, 190
- α -Methyl-5-hydroxytryptamine phosphate time course of changes in brain nuclei after injection, 194, 195
- α -Methyl-5-hydroxytryptophan, 194, 196
- α -Methyl-*p*-tyrosine, 436, 515, 518—519
- 3-Methylcholanthrene induction of hepatic oxidase activity, 215
- Methylphenidate, 605
- Methylscopolamine, 515, 518
- 6-Methyltetrahydro- β -carboline and changes in central serotonergic neurons, 284
- 6-Methyltetrahydropterin as cofactor in assay of tryptophan and tyrosine hydroxylases, 183
- Methysergide, 203, 204, 207, 284, 390, 406, 409, 458—459, 462, 498, 504—505, 515, 518—519, 539
 as inhibitor of serotonin-binding protein capacity, 91
 blockade of serotonin receptors, 623
 blocked myoclonic syndrome in rats, 511
 effects on serum values on the afternoon of estrus in rats, 403, 405
- inhibition of estrous rise of serum prolactin, 403
- pretreatment with neither enhances nor antagonizes 5,7-dihydroxytryptamine-induced hypothermia in rats, 489
- putative serotonin receptor antagonist, 485
- Monoamine oxidase, 11—12, 17—21, 470—471, 585. *See also* in sub-heads under other main headings, e.g. 5,7-Dihydroxytryptamine—metabolized by monoamine oxidase in rat hypothalamus homogenates
 and clearance of 5,7-dihydroxytryptamine from the brain, 116
 conversion of 5,6-dihydroxytryptamine, 40, 41, 54—55
 conversion of 5,7-dihydroxytryptamine, 40, 42, 54—55
 conversion of serotonin *in vitro*, 40, 43
 determination using [$1\text{-}^{14}\text{C}$]5,6-dihydroxytryptamine and [$1\text{-}^{14}\text{C}$]5,7-dihydroxytryptamine as substrates, 37
 effect of intracisternal injection of 5,6-dihydroxytryptamine in locus ceruleus of cats, 583, 585
 effect of *p*-chloroamphetamine on, 260
 inactivation by 5,6-dihydroxytryptamine or 5,7-dihydroxytryptamine, 53
 inactivation *in vitro* and *in vivo*, 38
 Michaelis constants and maximal velocities for conversion of 5,6-dihydroxytryptamine, 5,7-dihydroxytryptamine, and serotonin in rat hypothalamus, 40, 40
 time course conversion of 5,6-dihydroxytryptamine in rat hypothalamus, 39, 40
- Monoamine oxidase A, 48—49, 54
- Monoamine oxidase B, 49
- Monoamine oxidase inhibitors, 3—4, 19, 21, 74, 78, 81—82, 118, 254—256, 260, 307, 324, 347, 437—438, 481, 483, 486, 497, 520, 595, 600, 612—613, 664. *See also* Harmaline; 5-Hydroxytryptophan; Nialamide; Pargyline; Tranylcypromine
 affecting cytotoxicity of 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine differently, 56
 and neurotoxicity, 160

- Monoamine oxidase inhibitors—(cont'd)
and uptake of 5,7-dihydroxytryptamine, 171-172
kinetics of 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine, 41—42
protection against action of 5,7-dihydroxytryptamine, 167
- Monoamines, brain, 636, 637. *See also* in subheads under other main headings, e.g. 5,7-Dihydroxytryptamine—changes in brain monoamines and their metabolites induced in rats pretreated with harmaline or Lu 10-171
and their main metabolites, 616
catecholamines. *See* Dopamine; Norepinephrine
indoleamines. *See* 5-Hydroxyindoleacetic acid; Serotonin
- Morphine, 462, 488
effect on growth hormone release in rats, 422
- Morphine analgesia, effects of
5,6-dihydroxytryptamine, 541
5,7-dihydroxytryptamine, 541—542
6-hydroxydopamine, 541
fluoxetine, 541
in rats, 348
p-chlorophenylalanine, 541
selective electrolytic raphe lesions, 540—541
zimelidine, 541
- Mounting behavior. *See also p*-Chlorophenylalanine; Lu 10-171
after 5,6-dihydroxytryptamine or 5,7-dihydroxytryptamine in rats, 602, 616
after *p*-chlorophenylalanine in rats, 603, 613—614
classified as sexual behavior or not, 665
in rats, 596
serotonin neurons shown to originate in, 394
- Myoclonus
and cerebellar function, 260—261
drugs interfering with dopaminergic, norepinephrinergic, and cholinergic neurotransmission did not block syndrome in rats, 511
effect of serotonin antagonists produced by 5-hydroxytryptophan after 5,7-dihydroxytryptamine administration in rats, 511, 514
induced by *p*-chloroamphetamine, 518—520
record induced by 5-hydroxytryptophan in rats, 510, 513
syndrome related specifically to central indoleamine neurons, 511
- N**asoanal length in rats, 630, 636, 638
Neuroblastoma cells. *See* 6-Hydroxydopamine—and neuroblastoma cells
Neuroendocrine regulation and role of serotonin, 387, 394—395
Neurohumoral amine metabolic pathways, 182, 183
Neurons. *See* Catecholamine neurons; Dopamine neurons; Norepinephrine neurons; Serotonin neurons
Neurotoxic indoleamines. *See also* 5,6-Diacetoxytryptamine
cardiovascular effects, 457—474
degenerative effects on central monoamine neurons, 305—324
effects of various doses on brain and spinal cord serotonin and brain and spinal cord catecholamine content, 312—313, 312, 314
effects on monoamine levels, 312—313
effects on serotonin and norepinephrine uptake, 313—314
in vitro, 307, 307
fluorescence morphology, 315—317, 319
local intracerebral injections, 320—322
morphologic studies, 322—324
uptake site affinity and inhibition *in vitro*, 307—308, 309, 313
Neurotoxins. *See* 5,6-Diacetoxytryptamine; 5,6-Dihydroxytryptamine; 5,7-Dihydroxytryptamine; *o*-Dihydroxytryptamine; 6-Hydroxydopamine; α -Methyl-5,7-dihydroxytryptamine; Neurotoxic indoleamines; Serotonin-like neurotoxins
- Nialamide, 114, 117
as potentiating agent, 80
decreasing lordosis response frequency in female rats, 485
inhibiting conversion of 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine by monoamine oxidase, 47, 54
Nicotinic drugs and nicotinic receptors, 468
Nigrostriatal pathway, 524
model for interaction with other tracts, 530

- Nigrostriatal pathway—(cont'd)
modulation by striatal interneurons, 530
motor efferents, 530
- o*-Nitrotoluene, 25
- Nociception
analgesia, 488
hyperalgesia, 487—488
- Norepinephrine, 390, 393, 412, 418, 467, 477, 481, 490, 519—520, 576, 578, 582, 595, 602, 612—613, 624, 627, 665. *See also* in subheads under other main headings, e.g. Desmethylinipramine — blocking brain norepinephrine transport sites
- 5,7-dihydroxytryptamine effect on brain and spinal cord concentration in rats, 200
analyzed in forebrain of rats, 439—440
and specificity of 5,7-dihydroxytryptamine, 334, 336
appearing to be caused by an activation of presynaptic serotonin receptors on sympathetic nerve terminals, 462, 465
as neurotransmitter, 134
brain and spinal cord levels after treatment with 5,7-dihydroxytryptamine or *p*-chlorophenylalanine in rats, 498, 499, 503
catabolism, 21
concentration after administration of 5,7-dihydroxytryptamine in rats, 590—591, 592
concentration-response curve, 460
depletion by reserpine, 3
depletion in the heart, 135
effect of 5,6-dimethoxytryptamine on, 140
effect of 5,7-dihydroxytryptamine-induced lesions of serotonin pathways of midbrain on level in front of the lesion in rats, 355, 356
within cortex in rats, 354, 354, 356
effects of various drugs
and of calcium ion omission on output from isolated hearts and on the positive chronotropic effect evoked by 5,7-dihydroxytryptamine bolus injection in rabbits, 468, 469
on output from isolated hearts of rabbits, 468, 468
in brain, 402, 432—433, 540—541, 547
after intraventricular injection of 5,6-dihydroxytryptamine, 3—4, 146
cortex of rats, 365
hypothalamus, 406
long-term depletion, 20
of female rats, 621
of rats, 631, 638
telencephalon and diencephalon of rats, 349
turnover in rats, 252
influence of 5,7-dihydroxytryptamine on output and on increase in heart rate evoked by electrical stimulation, 469—470, 470
on removal of exogenous, by isolated hearts of rabbits, 469, 470
plus α -methyl-5,7-dihydroxytryptamine and desmethylinipramine on central nervous system, 14—16, 15
measured by radioenzymatic catechol *O*-methyltransferase method, 424
role in luteinizing hormone release, 388
substrate for monoamine oxidase, 48
uptake by atria in mice, 74—75
- Norepinephrine neurons, 107, 114—116, 337, 339—340, 342—343
lesions by 6-hydroxydopamine and regeneration of, 347
pathways in rats, 605, 612—613
pathways unaffected in rats, 603
regeneration after 5,7-dihydroxytryptamine or 5,6-dihydroxytryptamine treatment, 379, 383
regeneration after 5,7-dihydroxytryptamine treatment, 385
- Norfenfluramine, 120, 125, 150. *See also* in subheads under other main headings, e.g. 5-Hydroxyindoleacetic acid—brain concentration—after norfenfluramine administration in rats
as major metabolite of fenfluramine, 236
depletion of brain serotonin, 5-hydroxyindoleacetic acid, and tryptophan hydroxylase in rats, 150, 151
determination in plasma and brain by gas chromatography and gas chromatography-mass spectrometry, 224—225
mediator of long-term effect of fenfluramine, 236
method to differentiate from fenfluramine, 241

Norfenfluramine—(cont'd)

- plasma and brain concentration in rats, 225—226, 227, 228
- relation of brain concentration to depletion of serotonin, 222

Ontogenesis of serotonin neurons. *See* Serotonin neuron development

- Osmiophilia of serotonin organelles, 609, 609, 610

- Ovariectomy not affecting mounting behavior in female rats, 603

- Ovulation blocking by 5-hydroxytryptophan. *See* 5-Hydroxytryptophan—blocking of ovulation

Oxygen consumption. *See also* Antimycin A and oxygen consumption

- cyanide effect in brain mitochondria of rats, 79, 79, 81
- dopamine, serotonin, and boiled mitochondrial preparation, 79, 79, 81
- in brain mitochondria of rats, 75
- in brain mitochondria stimulated by 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine in rats, 79, 79, 81

- Oxygen reduction to form superoxide radical and ionized peroxide, 75, 75, 80

Pain sensitivity, effects of

- 5-hydroxytryptophan, 539—540
- 5,6-dihydroxytryptamine, 539
- 5,7-dihydroxytryptamine, 539—540
- and raphe lesions, 664—665
- electrolytic lesions in medial forebrain bundle, 539—540
- fluoxetine, 540
- p*-chloroamphetamine, 540
- p*-chlorophenylalanine, 539—541
- quipazine, 540
- tryptophan, 540

- Pancreas protection against alloxan by thiourea, 80

- Paraquinone of 6-hydroxydopamine. *See* 6-Hydroxydopamine

- Pargyline, 4, 17, 20, 203, 204, 502
- decreasing lordosis response frequency in female rats, 485

- effect on actions of 5,7-dihydroxytryptamine on newborn brain in rats, 165, 165

- effect on retention of rat brain radioactivity, 108, 110—111, 114, 116

Parkinsonism, therapy for. *See* L-Dopa

- Pentobarbital effect on growth hormone release in rats, 422

- Pentylenetetrazol inducing convulsions in mice, 437

- Pentylenetetrazol response after treatment with 5,7-dihydroxytryptamine or a raphe nuclei lesions in rats, 442, 443

- Perchloric acid, 5, 7, 9, 11—12, 20, 29, 38—39, 52, 53—54, 108, 110—111, 115—116

- Peroxidase, horseradish, 537

- Phenethylamine derivatives, autoxidizable. *See* 6-Hydroxydopamine

Phenobarbital, 438

- and β , β -difluoro-*p*-chloroamphetamine, 153

- and half-life of *p*-chloroamphetamine, 221

- effect of 5,7-dihydroxytryptamine or a raphe lesion on anticonvulsant action, 448—450, 452

- effect on maximal electroshock-induced hindleg extension in rats, 449, 449, 450

- induction of hepatic oxidase activity, 215

- Phenothiazines reducing receptor availability of neurotransmitters, 389

- Phenoxybenzamine, 515, 518

Phentolamine, 458

- 1-Phenyl-3-(2-thiazolyl)-2-thiourea

- as copper chelator, 84
- as hydroxyl radical scavenger, 82
- as protective agent, 80
- structure, 77, 77, 80—81

Phenylalanine, 546, 642

- Phenylalanine hydroxylase, 540, 546

- Phenylethylamine compound effect on protein synthesis, 96, 99, 100, 101

- 3-Phenylpiperidines, chlorinated, 153

Phenytol, 438

- effect of 5,7-dihydroxytryptamine or a raphe lesion on anticonvulsant action, 448—450, 452

- effect on maximal electroshock-induced hindleg extension

- after a raphe nuclei lesion in rats, 450, 450

- in rats, 449, 449, 450

Pimozide, 515, 518

- counteraction of hyperthermic effect of *d*-amphetamine, 252

Pindolol, 467

- Piperocaine, 623—624

- Piperonyl butoxide
 effect on reduction of serotonin and tryptophan hydroxylase by *p*-chloroamphetamine, 208, 209
 inhibition of hepatic oxidase activity, 215
- Piribedil, 605
- Pituitary-adrenal axis suppression by intraventricular injection of indoles, 392
- Pituitary, anterior, regulation of secretion, 387
- Platelets, blood. *See* Blood platelets
- Postural syndrome and *p*-chloroamphetamine-induced abnormalities, tremor, and myoclonus in rats, 511, 514
- Probenecid, 17
- Progesterone location of implants in female rats, 624, 624
- Progesterone uptake by all brain regions in rats and guinea pigs, 623
- Prolactin, 362—363, 389—390, 394, 400, 434
 in rat plasma, 436
 in rats, 630, 638, 641
 serum estrogen-induced surges blocked by *p*-chlorophenylalanine or methysergide, 399
 serum values on the day of vaginal estrus in rats, 402, 403
 stimulation of release after intracerebroventricular serotonin injection, after administration of 5-hydroxytryptophan and treatment with serotonin agonists, 399
 stress-induced release governed primarily by the norepinephrine system, 433
- Propranolol, 462, 515, 518
- Prostaglandins, 665
- Protein synthesis inhibition by neurotoxins, 96—104
- Protriptyline, 438, 595
 as norepinephrine uptake blocker, 346
 plus 5,7-dihydroxytryptamine as a means of selective lesioning serotonergic neurons, 439, 452
 pretreatment with, 543
 preventing the effects of 5,7-dihydroxytryptamine on norepinephrine neurons, 439
- Q**uinine sulfate
 acceptance of varying solutions instead of tap water by rats, 634, 635
 in drinking water for rats, 630
- Quinoid structures, 18, 29, 54
 of 6-hydroxydopamine, 36
- 1,4-*p*-Quinone derivative of 6-hydroxydopamine. *See* 6-Hydroxydopamine—1,4-*p*-quinone derivative of
- o*-Quinone
 of 5,7-dihydroxytryptamine, 21
 sulfhydryl group reduction, 103
- p*-Quinone
 sulfhydryl group reduction, 103
- p*-Quinoneimine of 5,7-dihydroxytryptamine, 19—21
 neurotoxicity, 55
- Quinoneimines from 5,6-dihydroxytryptamine or 5,7-dihydroxytryptamine, 53
- Quinones
 from 5,6-dihydroxytryptamine or 5,7-dihydroxytryptamine, 53—54
 neurotoxic effects, 175
- Quipazine, 207, 487
 producing myoclonic syndrome in rats, 511
 stimulation of serotonin receptors stimulating prolactin release, 389—390
- R**aphe nuclei
 dorsal raphe nucleus, 482
 in midbrain, 484—485
 in rats, 488—490
 lesions. *See also* Acetazolamide; Acetylcholine; Activity level; Avoidance behavior; Behavior, rotational; Brain; 5,7-Dihydroxytryptamine; Pain sensitivity, effects of; Pentylene-tetrazol; Phenytoin; Receptor supersensitivity; Spatial reversal learning
 producing behavioral and electrophysiologic signs of insomnia in cats, 483
 locomotor activity, 481
 median or dorsal, 489—490
 nucleus raphe dorsalis or nucleus raphe magnus, 487
- Rearing activity
 behavior of rats, 652, 652, 654, 655, 656, 657
- Receptor supersensitivity
 absence after median raphe nucleus lesions, 527
 due to serotonin or dopamine neurons in rat brain, 526
 Ungerstedt's model, 526—527

- Rectal temperature
 effect of 5-hydroxytryptophan in rats pretreated with desmethylinipramine and 5,7-dihydroxytryptamine, 511, 513
- Reserpine, 302, 437, 462, 467, 578. *See also* in subheads under other main headings, e.g. Norepinephrine—depletion by reserpine
 amine depletion with, 392
 and serotonin-binding protein, 95
 as inhibitor of serotonin-binding protein capacity, 86
 brain injected later with fluoxetine in rats, 229, 233
 reduction of thyroid-stimulating hormone with, 394
 uptake by atria
 5,7-dihydroxytryptamine, 5,6-dihydroxytryptamine, and norepinephrine, 62, 64, 71
- Reticulocyte ribosomes, 97
- Ribonucleic acid, globin messenger, 97—98
- RO4-4602, 203, 204
 correlation between the decrease in cortical 5-hydroxytryptophan and the decrease in striatal dopamine after injection of rats, 528, 528
 preventing conversion of 5-hydroxytryptophan to serotonin, 392
 to measure the turnover of dopamine and serotonin in rats, 525
- Rotational behavior. *See* Behavior, rotational
- Rotenone and oxygen consumption, 81
- S**alicylates and brain serotonin concentration, 92
- Schizophreniform symptoms, fenfluramine-induced, 490
- Seizure susceptibility changes, 456
 after intracerebral treatment with 5,7-dihydroxytryptamine, 437—453
 effect of 5,7-dihydroxytryptamine, 438—445, 447—448
 effect of a raphe lesion, 438—445, 446, 447—448
 electroshock seizures by corneal stimulation in rats, 442
 forebrain norepinephrine and dopamine concentrations unaltered in 5,7-dihydroxytryptamine-treated rats, 452
 induced by pentylenetetrazol by intra-peritoneal injection in rats, 441—442, 445, 452
 role of serotonin, 453
- Serotonergic elements, 242
 receptor supersensitivity, 243
 selective destruction, 263
- Serotonergic motor syndromes, 510—520
- Serotonergic nerve terminals, supersensitivity after destruction of. *See* Supersensitivity after destruction of serotonergic nerve terminals
- Serotonergic raphe inputs to the nigrostriatal pathway diagrammatic model, 529, 529
- Serotonin, 254—256, 422, 437—440, 442, 444—445, 447—448, 450, 452—453, 472, 497, 504—505, 530—531, 556, 568, 613, 616—617, 627. *See also* other main headings beginning "Seroton—" or with the word "serotonin" (e.g. 5,7-Dihydroxytryptamine and serotonin); *also* subheads throughout the subject index may refer to serotonin and should be sought by referring to related concept, as they are too numerous to list here (e.g. Brain—serotonin content; Hydroxyindole derivatives—and serotonin-binding protein)
- abnormal motor response complex induced by *p*-chloroamphetamine, 209, 211
- alterations in postnatal development of serotonin neurons after administration at birth, 339, 341
- analyzed in forebrain, brain stem, and spinal cord of rats, 439
- and mediation of hyperthermic response to *d*-amphetamine and apomorphine in rabbits, 252
- as neurotransmitter, 134, 483
- binding sites in lumbar spinal cord, 118
- brain and spinal cord levels after *p*-chlorophenylalanine and 5,7-dihydroxytryptamine administration, 511, 514, 514
- brain and spinal cord levels after treatment with 5,7-dihydroxytryptamine or *p*-chlorophenylalanine in rats, 498, 499, 503
- brain concentration, 152, 171
 after fenfluramine administration in rats, 231, 235
 after intraperitoneal injection of *p*-chloroamphetamine in rats, 515, 517

Serotonin—(cont'd)

brain concentration—(cont'd)

after norfenfluramine administration
in rats, 229, 234

after treatment with fluoxetine in
rats, 227, 228, 229

in forebrain and midbrain after fen-
fluramine administration in rats,
231, 237

in rats, 519

measured, 87—88

permanence of recovery induced by
fluoxetine in rats, 227, 230

spectrofluorometric assay, 400

brain concentration depletion

after injection of fenfluramine, 222

after injection of *p*-chloroamphet-
amine or *p*-chloro-*N*-methylam-
phetamine in rats, 150—151, 151
after intracisternal injection of 5,7-
dihydroxytryptamine, 4

and recovery in rat brain regions
after single intraventricular injec-
tion of 5,6-dihydroxytryptamine,
370, 371, 372

by *p*-chloroamphetamine in rats, 645
in whole brain by *p*-chlorophenylala-
nine and reversed by 5-hydroxy-
tryptophan in rats, 590, 592

long-term, 20

related to route of administration
used, 171

causing release of melanocyte-stimu-
lating hormone after administra-
tion in frogs, 394

chronic receptor blockade, 498

competition of unlabeled vs. tritium-
labeled *in vitro* in brain of rats,
337, 339

competition vs. *d*-lysergic acid diethyl-
amide for [³H]-*d*-lysergic acid di-
ethylamide *in vitro* in brain of
rats, 337, 340

depletion, 119

effect of 5,7-dihydroxytryptamine-in-
duced lesions of serotonin path-
ways of midbrain on level
in front of the lesion in rats, 355,
356

within cortex in rats, 364, 354, 356

endogenous in bulbospinal system given
injection of 5,6-dihydroxytrypt-
amine intraventricularly in rats,
372, 372

failure of depletion to prevent induced
prolactin rise in females treated
with 5,7-dihydroxytryptamine, 478

formation from tryptophan in different
central nervous system regions in
rats, 315, 318

history of isolation and characteriza-
tion, 1

importance of interval between injec-
tion of fenfluramine and fluoxetine
on recovery in brain of rats, 227,
232

in brain, 402, 411, 418—420, 432—434
activating the secretion of adrenocor-
ticotropic hormone, prolactin,
and growth hormone, 411

after injection of 5,6-dihydroxytrypt-
amine, 3—5

binding *in vitro* in rats, 337, 338

cortex in rats, 365

cortical uptake after fenfluramine
administration in rats, 231, 235

depletion having anorexigenic effect,
418—419

hypothalamus, 406

in rats, 631, 636, 638, 640—642

inhibits secretion of gonadotropins,
411

recovery produced by fluoxetine in
rats treated with norfenfluramine,
229, 230

reduced with *p*-chlorophenylalanine
plus 5,6-dihydroxytryptamine, 436
telencephalon and diencephalon in
rats, 349

time course of changes in nuclei
after injection of α -methyl-5-hy-
droxytryptamine, 194, 195

time course of changes in nuclei after
injection of *p*-chloroamphetamine,
192, 193

tryptophan-induced elevation, 392

uptake in rats, 334, 335

whole brain, 406

influence of 5,7-dihydroxytryptamine,
 α -methyl-5,7-dihydroxytryptamine,
and desmethylinipramine on cen-
tral nervous system, 13—14, 14

inhibition of surgery-induced adrenal
steroid secretion with intraventric-
ular doses in dogs, 392

intraventricular injection shown to in-
hibit gonadotropin release and to
stimulate prolactin release in male
rats, 423

long-lasting effect of fenfluramine,
234—235

maximal velocity, 48—49

Serotonin—(cont'd)

- mean concentrations after administration of 5,7-dihydroxytryptamine into rats, 590—591, 592
- measured by radioenzymatic hydroxyindole *O*-methyltransferase method, 424
- measurement by chromatography, 191, 191
- metabolic effects, 394
- Michaelis constant, 48
- microinjection into hypothalamus at room temperature raises body temperature in monkeys, 488—489
- monoamine oxidase-catalyzed conversion of tryptamine, 41, 48
 - inhibited, 41, 49
- nervous system regional differences, 213—214
- reduction of cerebrospinal serotonin accompanied by enhancement of sexual activity in male rats, 595
- release, 561
- role in mechanism of sleep in cats, 576
- storage and/or transport, 86—87
- synthesis rate, 234
- toxic inhibitory tone on gonadotropin release, 388
- uptake, 133
 - by synaptosomes, 92
- Serotonin analogs, 129—132
- Serotonin-binding protein
 - 5,6-dihydroxytryptamine and 5,7-dihydroxytryptamine as inhibitors of, 85
 - binding of newly synthesized serotonin, 92, 93
 - characteristics of capacity, 87
 - ferrous ion-enhancing capacity, 86
 - inhibition of serotonin binding by neurotoxins, 88—89, 88
 - location in synaptosomal cytoplasm and cytosol of brain and peripheral nervous tissue, 86
 - role of sulfhydryl group, 86
- Serotonin cell group (B1—B9) anatomy, 532—533, 533, 535, 536—537, 537—538, 544
 - afferent connections, 538—539
 - efferent projections from
 - dorsal raphe to amygdala, 537
 - dorsal raphe to caudate-putamen, 537
 - median raphe to individual hypothalamic nuclei, 537
 - median raphe to septum-hippocampus, 537
- Serotonin denervation hypersensitivity, 406
- Serotonin depletion methods
 - differences in neurochemical effects, 532
 - importance in determining behavioral effects, 532
- Serotonin inhibitors. *See* Lisuride maleate; Lu 10-171; Methysergide
- Serotonin-like neurotoxins, 129—132
- Serotonin neuron development, 329, 338—343, 346—350, 366
 - axonal sprouting in rats, 376
 - effects of neonatal 5,7-dihydroxytryptamine treatment in rats, 330—332, 334
 - growth regulation, 342
 - intracisternal 5,7-dihydroxytryptamine injection, 341—342
 - not associated with collateral sprouting of nerves not damaged by 5,7-dihydroxytryptamine, 342
 - route of neurotoxin administration, 328—329
 - serotonin receptors, 337, 342
- Serotonin neuron ontogenesis. *See* Serotonin neuron development
- Serotonin neurons, 107, 114—116, 573, 576, 582, 659—660
 - affecting behavior including sleep, feeding, temperature control, and pain sensitivity, 510
 - effect of 5,6-dihydroxytryptamine on, 346
 - effect of *p*-chloroamphetamine on in rats, 645, 649
 - evaluation of degeneration, 350—351
 - false neurotransmitter as tool for study of, 190
 - hyperresponsivity in rats after lesions, 363—364
 - in hypothalamus, 410
 - in rat brain, 642
 - in rats, 602, 605, 609
 - negative reinforcement, 363
 - regeneration after 5,7-dihydroxytryptamine or 5,6-dihydroxytryptamine treatment, 379, 383
 - regeneration in brain after
 - 5,6-dihydroxytryptamine-induced axotomy in rats, 370—383
 - 5,7-dihydroxytryptamine-induced axotomy in rats, 370
 - supersensitivity disappearing, as shown by reduced responsiveness to 5-methoxydimethyltryptamine and to tryptophan, 347

- Serotonin neurons—(cont'd)
 terminals as primary site of action of
 fenfluramine, 238
- Serotonin neurotoxins, 394—395, 409.
See also 5,6-Diacetoxytryptamine;
 5,6-Dihydroxytryptamine; 5,7-Di-
 hydroxytryptamine; *o*-Dihydroxy-
 tryptamine; 6-Hydroxydopamine;
 α -Methyl-5,7-dihydroxytrypt-
 amine; Neurotoxic indoleamines;
 Serotonin-like neurotoxins
- as tools to study thyroid function, 394
- Serotonin receptors, 457, 664
 newly synthesized serotonin, 86
 supersensitivity, 593
- Serotonin-secreting neurons, central, 457
- Serotonin system, ascending and progres-
 terone, 623—624
- [³H]Serotonin
 accumulation and retention in tissue
 slices, 308, 310—311, 310, 311
 binding in brain cortex after serotonin
 denervation of forebrain in rats,
 364—366
 binding in brain cortex of rats, 351,
 358—360, 358, 359, 360, 361, 362
 metabolism from [³H]tryptophan, 373,
 374—375, 376
 uptake in cortex and hypothalamus
 after 5,7-dihydroxytryptamine-
 induced lesions in rats, 356
 uptake in medulla oblongata and spinal
 cord after 5,6-dihydroxytrypt-
 amine treatment in rats, 372, 373
 uptake of total tritium and unchanged
 [³H]serotonin by brain slices and
 spinal cord in rats, 370, 371, 372
- Sexual behavior. *See also* *p*-Chloroam-
 phetamine; L-Dopa; Fenfluramine;
 Mounting behavior
 dependent on ovarian hormones estro-
 gen and progesterone appearing
 mediated by a serotonergic sys-
 tem, 624
 effect of intracranial hormone adminis-
 tration in female rats, 623, 623
 facilitated by norepinephrine in female
 rats, 622
 increased after injection of *p*-chloro-
 phenylalanine in rats, 485—486
 suppressed by serotonin in female rats,
 622
- Sleeping and waking, 481—484. *See also*
p-Chlorophenylalanine; 5,6-Dihy-
 droxytryptamine—as tool for
 studying sleep mechanisms in cats;
 Serotonin—role in mechanism of
 sleep in cats
 amount of paradoxical sleep after in-
 jection of 5,6-dihydroxytryptamine
 in cats, 578, 579
 amount of stage-2 sleep after injection
 of 5,6-dihydroxytryptamine in
 cats, 578, 579
 and hyperthermia in serotonin-infused
 fowl, 247—248
 and lesions of serotonin pathways with
 5,7-dihydroxytryptamine in rats,
 349, 365
 arousal, 480, 487
 brain serotonin neurons may play im-
 portant role in mediating, 480
 rapid eye movement, 483—484
 sedation and depression, 481—482
 slow-wave sleep, 484
- Spatial reversal learning effects of mid-
 brain raphe lesions, 545
- Spinal cord
 decrease in serotonin level in rats, 503
 in rats, 377
- Spleen
 norepinephrine level after single dose
 of 5,6-dihydroxytryptamine or
 3-(β -aminoethyl)-5,6-dihydroxy-
 benzo[b]thiophene in rats, 136,
 137
 serotonin level after single dose of 5,6-
 dihydroxytryptamine or 3-(β -
 aminoethyl)-5,6-dihydroxybenzo-
 [b]thiophene in rats, 136, 137
- Subcommissural organ
 after injection of 5,6-dihydroxytrypt-
 amine in rats, 267, 268, 279,
 280—281, 283
 after intraventricular injection of 5,7-
 dihydroxytryptamine in rats,
 272—273, 275, 276, 277
 and serotonergic synapses, 262—264
 apical process in contact with cerebro-
 spinal fluid after intraventricular
 injection of 5,7-dihydroxytrypt-
 amine in rats, 273, 275
 autoradiography, 265
 definition and location, 262
 detection of somatostatin, luteinizing
 hormone-releasing factor, thyro-
 tropin-releasing factor, and argi-
 nine vasotocin in, 283
 electron microscopic observations in
 rats, 265, 269, 270—271, 273
 fluorescence histochemistry, 264
 fluorescence micrograph of sagittal sec-
 tion from rats, 266, 266

Subcommissural organ—(cont'd)

- histochemical demonstration of nucleoproteins, glycoproteins, and neurosecretory proteins, 265
- increased extracellular space in hyalendyma after injection of 5,6-dihydroxytryptamine in rats, 275, 278
- indoleaminergic innervation confirmed, 284—285
- inhibitory effects of serotonin on protein synthesis, 284
- innervation, 282—283
- of rats as model for neuron-target cell interaction, 282—284
- perinuclear region of cells after intraventricular injection of 5,6-dihydroxytryptamine in rats, 273, 274
- protein and glycoprotein synthesis inhibited by serotonergic input, 264
- secretory function, 279—280, 282—283
- serotonergic terminals in the ependymal cells, 385
- serotonin terminals, 282—284
- varicose fluorescent fibers after intraventricular injection of 6-hydroxytryptamine in rats, 267, 268
- Subsensitivity after destruction of serotonergic nerve terminals affected by various doses of fenfluramine in injected rats, 501—502, 502
- Sucrose
 - acceptance of varying solutions instead of tap water by rats, 634, 634
 - in drinking water for rats, 630
- Sulfhydryl groups, 54, 56. *See also* 5,6-Dihydroxytryptamine—reaction with sulfhydryl groups; Serotonin-binding protein
- in peptides and proteins, 18
- Superoxide dismutase
 - inhibition of tryptamine conversion not antagonized, 41
- Superoxides
 - sites of action from neurotoxins, 84
- Supersensitivity after destruction of serotonergic nerve terminals
 - 5-methoxy-*N,N*-dimethyltryptamine, 497—498
 - 5,7-dihydroxytryptamine, 498, 500—502, 504—506
 - adenyl cyclase activity, 506
 - administration of L-tryptophan (after monoamine oxidase inhibition) and L-hydroxytryptophan both producing the syndrome, 497, 504—505

effect of various doses of 5-methoxy-*N,N*-dimethyltryptamine in injected rats, 500—501, 501, 504—505

effect of various doses of *d*-lysergic acid diethylamide in injected rats, 500—501, 501, 504—505

effect of various doses of L-5-hydroxytryptophan in injected rats, 500, 500, 503, 503

effect of various doses of L-tryptophan in rats, 501, 502

fenfluramine, 497, 504—505

p-chloroamphetamine, 497

presynaptic, 504

serotonin, 497

Sympathetic nerves of the heart, 457

decrease in norepinephrine content, 471

degeneration of the terminals, 471

in rabbits, 462

norepinephrine uptake, 469

serotonin causing norepinephrine release from, 468

Synaptosomal accumulation of serotonin in various brain regions in rats, 647—648

Temperature, body. *See also* *p*-Chlorophenylalanine; Hyperthermia; Hypothermia; Rectal temperature

average deviation in response to exposure to cold or warm air in rats, 559, 561

behavioral thermoregulation in monkeys, 564—566

deviation from a baseline after injection of 5,6-dihydroxytryptamine in monkeys, 562, 563, 565, 565

injection of saline and 5,6-dihydroxytryptamine in rats, 558, 560

intrahypothalamic injection of serotonin in monkeys, 558, 559

risk of exposure to cold and warm air after serotonin and saline injection and after 5,6-dihydroxytryptamine injection into anterior hypothalamus in rats, 561, 562

hypothalamic actions of serotonin neurotoxins, 573

maximum rise induced by serotonin injected into hypothalamus before and after 5,6-dihydroxytryptamine injections at the same site in rats, 558, 560

of monkeys after injection of 5,6-dihydroxytryptamine, 564, 564

regulation, 488—489

- Temperature, body—(cont'd)
 thermoregulatory mechanism
 after hypothalamic injection with
 5,6-dihydroxytryptamine, 559, 561
 deficits in monkeys and rats, 571—
 572
 in hypothalamus, 556—557
- Testosterone, 486
- Thiourea
 as protective agent, 80—81
 structure, 77, 77
- Thyroid C cells
 uptake of 6-hydroxydopamine, 56
- Thyroid-releasing hormone, 389
- Thyroid-stimulating hormone, 393—394
- Tibial length, right, in rats, 631, 636, 638
- Transmitter turnover
 correlations with rotational behavior,
 526
 dopamine turnover, 526
 serotonin turnover, 526
- Tranlycypromine, 510, 519
- Trazodone as inhibitor of serotonin-
 binding protein capacity, 91
- m*-Trifluoromethylbenzoylglycine
 recovery from rat brain as fenfluramine
 metabolite, 120, 122, 125—126
- Triton® X-100
 and oxygen consumption, 81
- Tryptamine, 387, 538, 540, 546, 664
 and excess concentration of 5,6-dihy-
 droxytryptamine, 5,7-dihydroxy-
 tryptamine, or serotonin to inhibit
 conversion, 49, 54
 in brain, 481
 noncompetitive inhibition by 5,6-dihy-
 droxytryptamine or 5,7-dihydroxy-
 tryptamine, 53
- Tryptamine derivatives
 acute toxicity, 458
 in isolated strips of rabbit aorta, 459,
 459, 461
 numbering system, 128, 129
- Tryptamines
 synthesis, 25, 27
- Tryptamines, hydroxylated
 effect on serotonin, norepinephrine, and
 dopamine uptake into hypothala-
 mic homogenates, 128—129, 130,
 131
 effect on serotonin uptake into hypo-
 thalamic homogenates, 128—129,
 129
- Tryptophan, 199, 203—205, 254, 389,
 391, 483, 519, 532, 576, 578, 642,
 664
 as precursor for serotonin, 510
 essential amino acid for serotonin bio-
 synthesis, 481
 in central nervous system, 4
 in diet, 487
 loading to increase neuronal serotonin
 levels, 394
 pretreatment with neither enhances nor
 antagonizes 5,7-dihydroxytrypt-
 amine-induced hypothermia in
 rats, 489
- Tryptophan hydroxylase, 153—154, 158—
 159, 182—184, 204, 259, 297, 437,
 532—533, 537—538, 540, 546,
 586, 621
 and *p*-chloroamphetamine, 208, 211,
 213—215, 217
 in rat brain, 649
 inactivated by *p*-chlorophenylalanine,
 519
 measurement by high-pressure liquid
 chromatography, 190
 reduced in brain by *p*-chloroamphet-
 amine in rats, 645
 time course of changes in brain nuclei
 after injection of *p*-chloroamphet-
 amine, 192, 193
- Tryptophan-induced neurologic syndrome
 myoclonus, 206—207
- Tryptophan-poor diets, 539—540
- Tubulin relation to serotonin-binding
 protein, 90—91
- Turning behavior. *See* Behavior, rota-
 tional
- Tyrosine, 583, 642
 in brain of cats, 578
- Tyrosine hydroxylase, 182—184, 221,
 255, 478, 540, 546, 589, 621
 effect of intracisternally injected 5,6-
 dihydroxytryptamine
 in locus ceruleus of cats, 583—584,
 585
 on activity in the locus and frontal
 cortex in cats, 582—583, 583, 584
 increase in activity in the locus ceruleus
 after bilateral injection of 5,6-di-
 hydroxytryptamine in cats, 585—
 586, 586
- Urethane anesthetizing of rats, 458
- Valine, 642
 injections, 487
- Vinblastine
 as inhibitor of serotonin-binding pro-
 tein capacity, 86
 effect on capacity of serotonin-binding
 protein in brain, 90, 91

Water intake. *See* Drinking

Weight, body. *See also* *p*-Chloroamphetamine; 5,6-Dihydroxytryptamine; Fenfluramine

after exposure to a high-fat diet instead of pellet chow in rats, 634, 635

average loss or gain in rats injected intraventricularly with 5,6-dihydroxytryptamine, 6-hydroxydopamine, or artificial cerebrospinal fluid and some given 5,7-dihydroxytryptamine similarly, 568, 570

changes in monkeys and rats, 566, 568

ethanol preference test obtained for 5,6-dihydroxytryptamine- and 6-hydroxydopamine-injected rats, 571, 572

gain accompanying overeating in rats, 571

gain in rats, 642

in rats, 627, 638, 640—642

loss or gain in rats after single injection of 5,6-dihydroxytryptamine, 5,7-dihydroxytryptamine, 6-hydroxydopamine, or cerebrospinal fluid in brain ventricle, 568, 569

obesity in rats, 627

regulation in rats, 628, 640, 642

Zimelidine, 352, 352, 353, 354—356, 355, 362, 645—646, 648—649, 651—660. *See also* in subheads under other main headings, e.g. Morphine analgesia, effects of—zimelidine

as potent serotonin uptake-blocking agent





Author Index

(Italicized page numbers refer to comments in discussions; boldface page numbers indicate abstracts.)

Ainsworth, E. J., 325-342

Allen, T., 199

Allison, A. C., 324, 367-370, 393, 427-428

Alving, C. R., 122-123, 233, 257, 365, 369

Atchison, M. L., 395-410

Bach, D., 385

Bangham, A. D., 2-7, 82-83, 100, 163, 182, 248, 266-267, 341-342, 367, 368, 424, 425

Barratt, D. G. 441

Basu, M. K., 198

Baurain, R., 226-234

Bennett, L. G., 8-28

Bergelson, L. D., 438

Bharucha, J., 325-342

Bittman, R., 441

Blackwell, B., 8-28

Blok, M. C., 85-100

Blumenthal, R., 183, 280, 385, 433

Boulanger, Y., 8-28

Butler, K. W., 8-28

Carballo, P. P., 200-214

Caride, V. J., 435

Carr, V. M., 200-214

Cerny, E. A., 438-439

Chapman, D., 67-84

Chester, D., 162

Clejan, S., 441

Cleland, L. G., 410

Cohen, B., 99

Dave, C., 371-386, 394, 436-437

Day, E. P., 437

Deamer, D. W., 250-258, 440

de Duve, C., 226-234, 423, 424

de Gier, J., 63, 85-100

Deprez-de Campeneere, D., 226-234

Deroo, P. W., 441

Derzko, Z., 437

Desnick, R. J., 232-233, 366-367, 432

Dingle, J. T., 435-436

Dombrose, F. A., 366

Dray, S., 433

Elsbarth, 198-199

Englehardt, 122

Finkelstein, M., 235-249

Fisher, J. A., 200-201

Garnick, M. B., 233

Giacomoni, D., 433

Gould, R. M., 162, 225

Grant, C. W. M., 441

Gregoriadis, G., 343-370, 384-386

Guilmette, R. A., 438-439

Hanson, W. R., 325-342

Hargreaves, W. R., 440-441

Haynes, D., 66, 234, 440

Haywood, A. M., 275-280

Heiss, A., 64

Henkart, P., 433

Henney, C. S., 434

Hill, M. W., 48-49, 64, 101-110,

Ho, J. T., 437

Hoffman, R. M., 438

Hoffstein, S., 235-249, 435

Hsia, J. C., 139-148

Huang, C., 29-49

Huang, L., 182, 224, 280, 439

Hunt, C. A., 342, 386, 410, 431-432

Ihler, G. M., 367

Jacobson, K., 437

Jaroslow, B. N., 325-342

Jewkes, R. F., 281-307

Jeyasingh, K., 281-307

Jonah, M. M., 435

Jones, N. C., 215-225

Joyce, A., 8-28

Juliano, R. L., 411-425

Kalman, T., 257, 393

Kang, C. H., 440

Kantor, H., 162

Kataoka, T., 387-394

Kelly, R. B., 439-440

Kimelberg, H., 248-249, 395-410
 Kinsky, S. C., 111-123, 137, 138, 147,
 369, 394
 Knight, C. G., 435-436
 Kobayashi, T., 387-394
 Korchak, H., 235-249
 Kunze, R. K., 437

Lajtha, A., 182, 183
 Lampert, M. A., 65
 Landsberger, F., 183, 273, 436
 Laughlin, R. G., 233, 258
 Lavelle, L., 433
 Layton, D., 83
 Lettman, 163
 Lewis, J. T., 124-138
 Lowe, J. S., 435-436
 Lyles, D. S., 436

MacDonald, R. C., 65-66, 200-214,
 248, 258, 273, 274, 370
 MacDonald, R. I., 200-214
 Macek, C. M., 435
 Magee, W. E., 308-323
 Margolis, L. B., 438
 Mason, J. T., 29-49
 Mayhew, E., 371-386, 436-437
 McConnell, H., 6-7, 26-28, 64, 100,
 122, 124-138, 147, 160
 McCullough, N., 411-425
 McLaughlin, S., 63, 64
 Metcalfe, J. C., 65
 Mihich, E., 365-366, 394, 409-410, 428-
 429
 Mombers, C., 85-100
 Murphree, S. A., 438

Osborn, M. J., 160, 161, 163, 164, 182,
 215-225
 Osborne, M. P., 281-307
 Oster, K., 83, 162, 437-438
 Ostro, M. J., 433
 Ozato, K., 434

Pagano, R. E., 185-199, 280, 370
 Pangborn, W., 50-66
 Papahadjopoulos, D., 1, 50-66, 99, 121-
 122, 147, 148, 160-161, 164-184, 198,
 225, 247-248, 259-267, 268-274, 369-
 370, 371-386, 394, 426-427, 436-437
 Patel, H. M., 281-307
 Peel, W. E., 67-84
 Peria, 306

Phillips, N. C., 435-436
 Portis, A., 50-66
 Poste, G., 164-184, 199, 232-234, 248,
 280, 365
 Pownall, H. J., 257
 Preisler, H., 429-431

Quinn, P. J., 67-84

Rader, R., 123
 Rahman, Y. E., 325-342, 439
 Richardson, V. J., 281-307
 Ritchie, A. K., 439
 Ritter, C., 434-435
 Roerdink, F. H., 306, 410, 433-434
 Rogers, J. D., 441
 Rosenthal, A. F., 441
 Ross, D. J., 437-438
 Rustum, Y. M., 371-386, 436-437
 Rutman, R. J., 434-435
 Ryman, B. E., 281-307

Sandra, A., 185-199
 Sartorelli, A. C., 438
 Scherphof, G. L., 433-434
 Schindler, M., 215-225
 Schreier, S., 8-28
 Shafer, D., 49
 Sharnick, S., 437-438
 Sharom, F. J., 441
 Sharrow, S. O., 433
 Shaw, I. H., 435-436
 Smith, I. C. P., 8-28, 48, 49
 Smolen, J., 235-249
 Stamp, D., 411-425
 Stockton, G. W., 8-28
 Strong, P. N., 83, 439-440
 Sun, S.-T., 437
 Szoka, F. C., Jr., 437

Taber, R., 268-274
 Takeichi, M., 185-199
 Tan, C. T., 139-148
 Tattersall, M. H. N., 281-307
 Thomas, D. P. P., 435-436
 Thompson, T. E., 49, 100, 441
 Tom, B. H., 435
 Tracy, T., 394
 Tritton, T. R., 438
 Trouet, A., 226-234
 Tulloch, A. P., 8-28
 Turcotte, J., 385
 Turner, E. H., 435-436
 Tyrrell, D. A., 281-307

Vail, W. J., 259-267

Valder, L., 234, 387

van Deenen, L. L. M., 85-100

van der Neut-Kok, E. C. M., 85-100

van Dijck, P. W. M., 85-100

Verkley, A. J., 85-100

Vogl, S., 385, 394

Waite, M., 198, 233

Webb, W., 137-138

Weinstein, J. N., 120, 147, 197-198, 225,
273-274, 306, 423-425, 433

Weissmann, G., 120, 121, 136, 137, 224-

225, 235-249, 307, 323, 324, 368-369

White, A., 161

Wilson, T., 268-274, 279-280

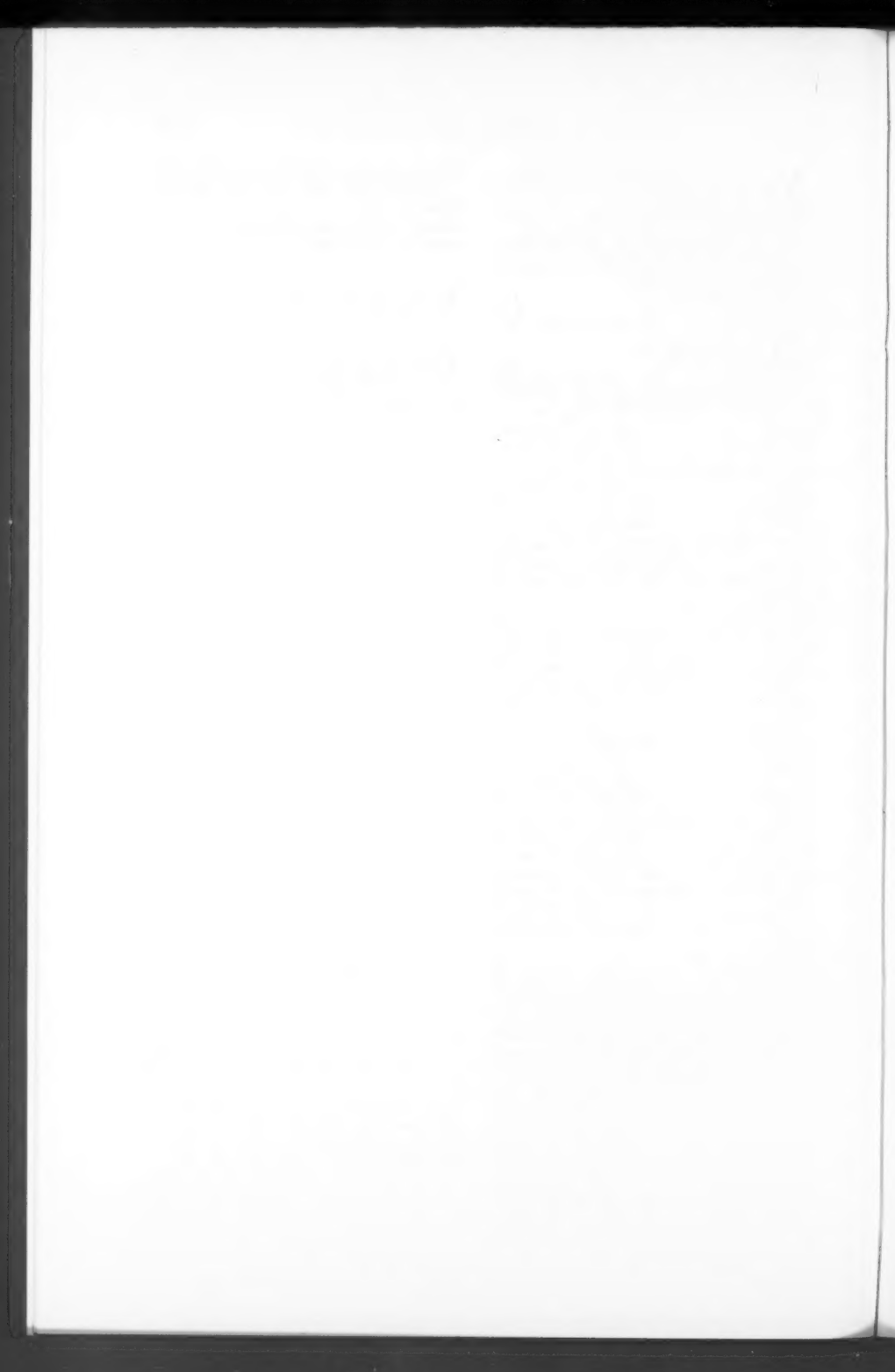
Wisse, E., 433-434

Yatvin, M. B., 83-84

Zaret, B. L., 435

Zeigler, H. K., 434

Zilversmit, D. B., 149-163



Subject Index

- Acanthamoeba castellanii**, endocytosis in, 167, 238–239
- Acholeplasma laidlawii**:
¹³C nmr of, 11, 15
 cholesterol effects on, 24, 96
 deuteration of, 22–24
 gel-state viability of, 86
 liquid-gel transitions in, 24
 quadrupole splittings in, 24
- Actinomycin D**:
 in antibody-forming cell production, 334–335
 antitumor effectivity of, 325
 DNA synthesis inhibition by, 332–333
 effects of, in female mice, 331–332
 immunosuppressive effects of, 337
 hematologic uptake, 327
 intestinal epithelial cells and, 332
 liposomal entrapped, 326, 350, 416–419
 cytotoxicity of, 252, 328–339
 lymphotoxic effects, 336–337
 target specificity role of, 308–309, 320–321
 toxicity of, free and entrapped, 328–336
 toxic side effects of, 325
 uptake and tissue distribution of, 326–329
- Acyl chains**:
 Ca ion effects on, 52, 58–59
 of egg PC, 30
 fatty, *see* Fatty acyl chains
 Mg ion effects on, 58
- Adriamycin**, 228–229, 233, 238, 413
- Adsorption**:
 cell microvilli in, 187–188
 cell surface proteins in, 192, 406; *see also* Exchange proteins
 fusion distinguished from, 171, 182; *see also* Fusion
 of gastrointestinal, nonabsorbable substances, 296, 298
 immunoglobulin in, 126–129, 237–238
 in liposome-cell membrane interactions, 166, 169; *see also* Liposome-cell interactions
 by mammalian cell surfaces, 187, 189
 metastability and, 197, 198
 phospholipid release in, 192
 proteolytic enzymes in, 189–190
 techniques in establishing, 189–199
 of vesicle components, 173, 176, 178
 of viruses, by liposomes, 276–277
- Agglutination**, 200, 201, 205, 212
- Aging**, phospholipid oxidation and, 83
- Alcohol(s)**:
 partition coefficients of, 104–105
 synaptic membrane polarization effects, 106–108
- Amphiphilic substances**:
 characterization of, 3–4, 412
 liposomal entrapment of, 414–419
- Amyloglucoside**, 282–283
- Amyloglucosidase**, 346
- Anesthetics**, general, *see also* Local anesthetics
 cation permeation and, 101, 102
 gas solubility and, 101–102
 Gibbs free-energy hypothesis of, 102, 109
 liposome as working model for, 101, 109
 Meyer-Overton rule of, 102
 organic solvent permeation and, 101
 partition coefficient of (K), 103–104
- Anhydrous solute molecule**, 35–36
- Antibodies**:
 antinitroxide specific, 124–129
 complement depletion by, 124–127
 in complement fixation, 126
 diagnostic, liposomes in production of, 115
 in entrapped antigen response, 353
 entrapment and synthesis of, by act D, 337, 338
 immunoglobulin (Ig) and, 127–129, 317, 318
 liposomes and, 115, 140–141; *see also* Immune response; Liposomes
 in monocyte lysis, 129
 specificity of, in lymphocyte activation, 317–321
 viral resistance to, via encapsulation, 269
- Anticancer chemotherapy**, *see* Antitumor chemotherapy
- Antigens**:
 haptens and, *see* Haptens
 lateral distribution of, 124
 lipid, in liposomal immunity, 111
 lipid linked, as sensitizer, 139–140
 liposome-entrapped, 299–300, 353
 liposomes and, in antibody response, 338
 in lysis measurement, 142, 147
 tumor specificity of, 429

Antitumor chemotherapy:

- actinomycin D in, 325-342
 - adriamycin in, 228-229, 413
 - daunomycin as, 338, 349, 412, 414
 - drug carrier liposomes in, 281-307, 328-338, 349-359, 387-389, 391-392, 402-403
 - drug types in, 412-416
 - encapsulation of drugs in, 325-339, 402-406, 412-419
 - human considerations in, 359-361, 366, 426-432
 - immunosuppressive variables in, 338
 - in vivo* drug administration in, 426-429
 - in vivo* inhibitory factors in, 387
 - liposomal enhancement in, 387-389, 392
 - requirements of, in general, 343
 - respiration systems therapy in, 418-419
 - side effects in, 325
 - single massive versus sustained release drug administration in, 429-430
 - S-phase specific drugs in, 420-423; *see also* DNA synthesis inhibition
 - toxicity of drugs in, 325, 328-338, 402-403
 - vinblastine in, 337, 412, 414
- Antiviral resistance, 311-314
- Aqueous phase liposomes (APL), 326-329
- Apparent fusion index (AFI), 205
- Arabinofuranosylcytosine (ara-C), *see* Cytosine arabinoside (ara-C)
- Arabinosylcytosine (ara-C), *see* Cytosine arabinoside (ara-C)
- Arabinosyl-5-fluorocytosine, 2,2'-anhydro (AAFC), 381
- Arabinosyl-5-fluorouracil, 1- β -D, 381
- Artificial membrane systems, 2-8; *see also* Bilayer lipid membranes; Model membrane systems
- Arzobenzeneearsonic acid (ABA) compounds, 114-115
- Asparaginase, liposomal carriers and, 350-352
- Aspergillus niger* amylglucosidase, entrapment of, 345
- Asymmetric membranes:
- in biomembranes, 157-158
 - exchange protein approach to, 156-157
 - nmr spectroscopy of, 157
 - in microsomes, 162
- Asymmetric vesicles:
- in liposome-cell membrane interaction, 194-196, 199
 - preparation of, 194-195

Aureobasidium pullulans, membrane properties of, 11-15

Bacteria:

- membrane structure of, 215
 - phospholipid transfer in, 215-219
- BCG (*Bacillus Calmette-Guérin*), 430-431
- Behenoyl-ara-C, potential chemotherapeutic utility of, 391, 393
- Bilayer lipid membranes, *see* Lipid bilayer membranes
- Binding:
- of bivalent metallic ions, 51, 57
 - of calcium ion, 55, 57, 63-65
 - in carrier liposomes, *see* Encapsulation
 - cell-surface proteins in, 192-194
 - of Fc stems and monocytes, 132-133, 137
 - ligand-induced capping and, 173, 174
 - in liposome-cell membrane interaction, *see* Adsorption; Fusion; Liposome-cell membrane interaction
 - of local anesthetics and lipids, 20
 - of magnesium ions, 50-57
 - of viruses and liposomes, 275-277
- Biological membranes:
- calcium ion activity in, 50-56, 175-176, 395
 - fluidity in, *see* Biological membrane fluidity
 - fusion in, 50-56
 - growth temperature and permeability of, 87
 - immunologic approaches to, with liposomes, 111-122
 - lipid bilayer resemblances of, 85
 - liquid-gel transition in, 27
 - local anesthetics and permeability of, 19
 - phase transitions in, and cell functions, 75-76
 - phase transition temperature in, 50, 53-56, 68, 85-87
 - phospholipid translocation mechanisms in, 156-157, 163
 - polypeptide roles in, 67-75
- Biological membrane fluidity:
- adaptation of, by organisms, 82-83
 - bond saturation and, 84
 - cholesterol effects on, 79-80
 - factors changing, 76
 - hydrogenation of, 76-80
 - phase change temperature and, 86
 - polypeptide-lipid contiguity in, 83

- Biological Transport, Symposium on Biophysics and Physiology of (1965), 5
- Biomembranes, *see* Biological membranes
- Birefringence, 2
- Bivalent cations, *see also* Calcium ions; Magnesium ions
binding ratios of, 57
effects on phospholipids, 50-60
- Blebs, 129-130, 205
- Blood-brain barrier, 284
- Bone marrow cells:
actinomycin D toxicity to, 329, 336
actinomycin D uptake by, 326-329
Technetium-liposome uptake by, 289
- Bordetella pertussis*, 353
- Boundary layer effect, 72
- Bound water, 38-40
- Brain tissue, toxicity of phospholipids in, 284-285
- C** aeruloplasmin, 347
- Calcium ions:
acid phospholipids and, 51-53
binding of, 55, 57, 63-65
in exocytosis, 61
fusion induction by, 50-56, 61, 65, 175-176, 178, 182, 395
isothermal phase transition and, 52-53
in large unilamellar PS vesicles, 260, 265
in lateral phase separation, 178, 217
in liposome-cell membrane interactions, 176, 178, 182, 216-219
in permeability, of lipid bilayers, 90-92
in phase separations, 51-52, 56, 90-92
in secretion, 61
structural changes in liposomes due to, 58-59, 89-90
- Cancer chemotherapy, *see* Antitumor chemotherapy
- Candida utilis*, 11
- Capping, of vesicle-derived ligands, 173, 174
- Carbon-13:
in enriched acetate method, 11-16
fatty acid labeling with, 12-15
lipid labeling with, 11-15
mobility values of, 12-15
in nuclear magnetic resonance (nmr), 8-9, 11-16
relaxation time of, 10-11
- Carbon-14, tissue uptake of, 396-402, 405
- Carboxylfluorescein, 129, 130, 147
- Carcinomas, carrier liposomes in treatment of, 281-307, 349-354; *see also* Antitumor therapy
- Cardiolipin, 3, 150, 393
- Catalytic hydrogenation, 76-80
- Cations, liposome permeation by, in anesthesia, 101-102; *see also* Bivalent cations; Monovalent cations; and specific kinds by name
- Cell(s), biological
agglutination of, 200, 201
antibody responses to, 114, 115
bacterial, *see* Bacteria; *Salmonella*
endocytosis by, *see* Endocytosis
erythrocytes as, *see* Erythrocytes
fusion within, *see* Cell fusion
fusion with liposomes, *see* Fusion
lipid vesicle uptake and incorporation by, *see* Liposome-cell membrane interaction
malignant, 79-80
proliferation regulation of, 431
- Cell fusion, 200-214
- Cell-mediated immunity, 114
- Cell membranes, *see* Biological membranes
- Cell phase specificity, of encapsulated drugs, 420-421, 423
- Cell surface proteins, 192-194; *see also* Exchange proteins
- Cephaein, *see* Phosphatidylethanolamine
- Cerebrosides, 3
- Chalones, 431
- Chemical labeling agents, in liposome-cell membrane exchanges, 157-158
- Channels, transmembrane, 68
- Chemotherapy, *see* Antitumor chemotherapy
- Cholesterol:
in asymmetric vesicle uptake, 195
in catalytic hydrogenation, 77-79
fatty acid chain effects of, 18-19
in DPPC phase transition, 72
erythrocyte membrane and, 97
gauche conformation effects of, 68-69, 94
in exchange reactions, 170
immunogenic effectiveness of, 392
in malignant cell control, 79-80
permeability effects of, 94-96
in phase-change enthalpy, 74, 94
phospholipid immune responses and, 118-119
phospholipid mobility and, 93-94
preferential affinities for, among phospholipids, 96-97, 100

Cholesterol—Continued

- random arrays of, in lipid chains, 73–74
- in *Salmonella* membranes, 221
- tissue uptake and clearance of, 396–402, 405, 406
- in virus-liposome fusion, 277
- in volume-trapping efficiency, 253, 254
- Circulatory system, carrier liposomes and, 416–417
- Closed membrane theory, 2–3
- Clostridium perfringens* neuraminidase, 345
- Cochleate cylindrical structures, 52, 53, 90, 91, 260, 265, 268
- Colony stimulating factor, 431
- Complement:
 - cascade of, 128
 - depletion of, 124–129
 - antinitroside antibody in, 124–127
 - hapten lateral mobility in, 126
 - fixation of, 126–127
 - immunoglobulins and, 126
 - recognition component activation, 127
 - in target membrane activation, 128–129
- Conformational changes, in membrane lipid molecules, 9–10
- Corynebacterium parvum*, 431
- Cytolysis, extracellular, 134
- Cytosine arabinoside (ara-C) (Arabinosylcytosine):
 - in carrier liposomes, 371–382, 387–389
 - enhanced effects in SM/SA/Chol carrier, 389–391
 - cell phase specificity of, 389–390, 391
 - cytotoxicity of, 376–380
 - enzymatic degradation of, 376–377, 389
 - in DNA synthesis inhibition, 375, 412, 420–421
 - liposome entrapment and leakage, 414, 416–419
 - therapeutic effects, free versus encapsulated, 389–391
 - time-sustained release of, 385–386, 390–391
 - tissue uptake of, 375–378
- Cytosine triphosphate arabinoside (ara-CTP);
 - in carrier liposomes, 371–382
 - cytotoxicity of, 378–381
 - DNA synthesis inhibition by, 375–376
 - encapsulation of, 373, 376, 278
- Cytotoxicity:
 - in antitumoral chemotherapy, 325, 328–338, 402–403; *see also specific drugs by name*

- carrier liposome characteristics and, 350–353, 360, 376–378, 382, 402–403
- in CNS, of liposomes, 284–285
- enhancement of, by encapsulation, 328–338, 353–354, 376–378, 380–381, 385, 426
- ionic charges on liposomes and, 285, 376, 378, 381, 392

- D** aunomycin, 338, 349, 412, 414
- Daunorubicin, 228–229
- DNA complex with, 228–229
- DEAE-dextran, 311, 314
- Deoxyribonucleic acid (DNA), *see also* DNA actinomycin D and, 332–333
- cytosine arabinoside (ara-C) and, 371–386, 412, 420–421
- cytosine triphosphate (CTP) and, 371–386
- as drug-molecule carrier, 228, 233–234, 328, 349
- as lysosomotropic-agent carrier, 228–229
- synthesis inhibition of, 332–333, 371–376, 379, 381, 421
- Deuterium, in membrane properties analysis, 8–28
- Diacytosis, 230
- Diffusion coefficient, 34–35
- Dimyristoyl phosphatidylcholine (DMPC), 88; *see also* Phosphatidylcholine
- Dinitrophenyl phosphatidylethanolamine (DNP-PE), and derivatives, 112–119, 142; *see also* Phosphatidylethanolamine
- Dioleoyl phosphatidylcholine (DOPC), in liposome immunity response, 118; *see also* Phosphatidylcholine
- Dipalmitoyl lecithin, *see* Dipalmitoyl phosphatidylcholine (DPPC)
- Dipalmitoyl phosphatidylcholine (DPPC):
- C-13 mobility of lipids in, 12, 14
 - deuterium nmr studies of, 16
 - liposomes of, preparation, 252
 - as partition coefficient model, 103–106
 - in phase separation, mixed membranes, 56
 - phase transition enthalpy in, 70–72
 - potassium ion leak and, 88
 - volume trapping efficiency of, 253–255
- Dipalmitoyl phosphatidylglycerol (DPPG):
- in calcium-ion-induced fusion, 55
 - in mixed lipid-water transition, 72–73

- Dipalmitoyl phospholipids, sonication and transition temperature in, 169
- Distearyl phosphatidylcholine (DSPC):
immunity response of, 118
in phase separation, mixed membrane, 56
x-ray differentiation spacing of, 57
- Divalent cations, *see also* Calcium ions;
Magnesium ions
binding specificity of, 51
in lipid incorporation by cells, 216
lipid vesicle changes due to, 90-91
phase transition temperature shifts and, 90
- DNA, *see* Deoxyribonucleic acid (DNA)
- DNA-actinomycin complex, 228, 229, 234
- DNA-daunorubicin complex, 228, 229
- Drug administration:
animal studies of, 429-430
of antitumor drugs, 412-416; *see also* Antitumor chemotherapy
carrier liposome characteristics and role in, 259, 344-345, 355-359, 376-378, 431-432
developments in, 344-346, 357-359, 365, 426-431
in vivo problems of, 239-245, 426-439
sustained versus intermittent release in, 371, 380-381, 385-386, 390-391, 429-430
- E**DTA, *see* Ethylenediaminetetraacetic acid
- Egg lecithin, *see* Egg phosphatidylcholine
- Egg phosphatidylcholine, 29-49, *see also* Phospholipid vesicles
acyl chain composition of, 30
beef sphingomyelin vesicles compared with, 117-118
cholesterol effects on, 17-19
deuterium nmr of, 16-19
endocytosis of, 167, 168, 187
fluorescence depolarization in, 109
homogeneity computation for, 33-34
hydration computations for, 40-42
immunogenic responses with, 117-118
intrinsic viscosity calculation for, 35
isolation of, 29-30
lipid molecule packing geometry of, 29, 43-46
partial specific volume calculation for, 35-36
plasma membrane fusion with, 167-168
preparation of, 29-30, 185
procaine binding with, 20
sedimentation coefficient of, 32
trapped volume calculations for, 37
volume trapping efficiency of, 253-254
- Electron paramagnetic resonance (epr), *see* Electron spin resonance (esr)
- Electron spin resonance (esr):
applications of, 8, 10, 139
of fatty-acyl chain conformations, 10
of polypeptide-lipid systems transition, 69-73
in spin-membrane immunoassay (SMIA) applications, 139-146
- Encapsulation, liposomal:
of actinomycin D, *see* Actinomycin D
of antitumor drugs, *see* Antitumor chemotherapy
of cytosine arabinoside (ara-C), *see* Cytosine arabinoside (ara-C)
of cytosine triphosphate (CTP), 380, 385
in drug administration, *see* Drug administration
drug effectiveness and, *see* Cytotoxicity of enzymes, 236-237, 345-347
in enzymes, 236-237, 345-347
in enzyme replacement therapy, 282-283, 347-349
in vivo effectiveness of, 265, 402-406
liposomal aspects of, *see* Liposomes of macromolecules, 259-267
mechanisms of, 414-415
metabolic breakdown and, 397-401
of poliovirus, 268-269
of polyribonucleotides, 308-324
potentials for, by vesicle size and type, 259
release from, *see* Sustained release
sonicated release of, 415
Tissue uptake and, *see* Tissue uptake
viral infection capability and, 269-271
volume and, *see* Vesicle-trapped volume
of water, *see* Water, encapsulated
- Endocytosis:
characterization of, 346, 395
in egg PC vesicles, 167-168, 187
fluidity of membrane and, 167
fusion as distinguished from, 427
immunoglobulins and, 237-240
inhibition of, 167-169
of liposomes by cells, 164-167, 173, 176-178, 230; *see also* Liposome-cell membrane interaction

Endocytosis—Continued

- of lysosomotropic carriers, 226–227, 230
- of negatively charged vesicles, 238, 412
- as sustained release mechanism, 386
- temperature dependence in, 170

Enthalpy, in phase change, 70–71, 74

Entrapment:

- of drugs by liposomes, *see* Encapsulation
- of liposomes by cells, *see* Fusion;
- Liposome-cell membrane interaction
- by organs and tissues, *see* Tissue uptake

Enzyme(s):

- in adsorbed phospholipid release, 189–193
- encapsulation of, 236–237, 345–347
- as liposome markers, 141
- replacement of, *see* Enzyme replacement therapy
- in targeting liposomes, 235–249
- Enzyme replacement therapy (ERT):
- drug carrier liposomes in, 235–236, 346–349
- in glycogen storage disease (Pompe's), 282–283, 298

Erythrocyte(s):

- agglutination of, 201, 205, 212
- ballooning of, 205–214
- ghosts of, *see* Erythrocyte ghosts
- substances effecting liposomal fusion with, 202–209

Erythrocyte ghosts:

- as drug-carrier liposomes, 367
- liposome fusion with, 202, 209

Erythropoietin, 431

Escherichia coli, 87

Esr, *see* Electron spin resonance

Ether-injection liposome production, 250–258

Ethylene diaminetetraacetic acid (EDTA):

- in cell fusion enhancement, 212
- in phospholipid preparation, 252, 260, 263
- in virus-liposome fusion, 276
- Exchange protein(s), phospholipid:
- adsorption and fusion in, 160–161
- beef brain, 150, 158
- beef heart, 149–150, 158
- beef liver, 149–150
- in biological membrane transfer, 157
- characterization of, 149–150
- in erythrocytes, 163

ion leakage and, 162

kinetic studies of, 161

lipid membrane asymmetry of, 152–153

in liposome-cell membrane interaction, 192–195

microsomal membranes and, 153–156, 162

net exchange and, 149

nonspecificity of, 150–154

properties of, by sources, 150

radiolabeling of, 192

rat liver, 149, 150, 158

Exocytosis, 60–61, 230–231; *see also* Liposome-cell membrane interaction

Fatty acids:

- carbon-13 labeling of, 12, 13, 15
- cholesterol and, 18–19
- oxidation of, and aging, 83
- synthesis of, 11, 12, 15

Fatty acyl chains:

- in amphiphilic drug entrapment, 415
- carbon-13 mobility values in, 12–14
- cholesterol effects on, 18–19
- conformational changes in, 9–10
- schematic of, 9
- segmental changes in, 10

Fatty-acyl residues, catalytic hydrogenation of, 76–80

Fc receptors:

- immunoglobulin (IgG)-coated liposome uptake by, 237–240
- in monocyte-immunoglobulin (IgG) molecule binding, 132–133, 137

Ferritin, 263

Fluorescence:

- in fluorescein loaded vesicles, 130–131, 168
- in liposome-cell membrane interactions, 167, 202, 204
- in liposome-t-cell adsorption, 189
- Fluorescence depolarization, 108–109
- Fluorodeoxyuridine (FUDR), 413, 419, 421

Fluorogenic substrates, as liposome markers, 141

F protein, in viral-liposome fusion, 278

Freeze-fracture, of liposomes, 253, 260–263

Frictional coefficient, for phospholipid bilayers, 39

Fusion:

among cells, *see* Cell fusion

- Fusion—Continued
 among lipid bilayers, *see* Lipid bilayer - fusion
 between liposomes and cell membranes
 see Liposome-cell membrane interaction
- Fusogenic agent(s):
 cell-shape effects of, 204
 characterization of, 200–201
 EDTA as, 212, 276
 gramicidin A as, *see* Gramicidin A
 in liposome-cell membrane interaction, 200–209
 in vesicle-cell lipid uptake, 239
- G**angliosides:
 in enzyme replacement therapy, 235, 284
 in liposome uptake, 406
 as viral receptors, in liposomes, 275–277
- Gauche* conformations, 18–19, 68–69
- Gaucher's disease, carrier liposome treatment in, 347, 348, 356, 365
- Gel-liquid crystalline transition, *see* Phase transitions
- Gibbs free-energy hypothesis, of anesthesia, 102
- Glucose:
 degradation to acetate, 11, 12
 as liposome marker, 141
- Glucocerebrosides, carrier liposome administration of, 347, 366, 367, 432
- Glycogenosis, type II (Pompe's disease), carrier liposomes in treatment of, 282–283, 298
- Glycolysis, 168
- Glycophorin, 72, 420
- Glycoproteins, as viral receptors, 275, 276
- Golgi system, 231
- Gramicidin (G):
 cell fusion effects of, 204–205, 209, 212
 in lipid molecule transitions, 68–69, 72
 in transmembrane channel formation, 68
- H***alobacterium cutirubrum*, 15
- Haptens:
 antigens and, 113, *see also* Antigens
 in complement depletion, 128, 129, 135
 in complement fixation, 126, 127
 in immune responses, 124, 126
 immunoglobulins and, 126–127, 129
 lateral mobility of, 124–128, 135, 137
- Hapten II, 129
- Hemagglutination, 276
- Heterogeneity parameter, 33, 34
- Hexosaminidase A, 284
- HN proteins, 279
- Human clinical administration, of carrier liposomes, 359–361, 365, 426–431
- Hydrodynamic analysis, of phospholipid bilayers, *see* Egg phosphatidylcholine; Lipid bilayer vesicles
- Hydrogenation, catalytic, 76–80
- Hypersensitivity reactions, 353
- I**gM, *see* Macroglobulin
- Immune response, liposomal:
 bilayer fluidity and, 119
 cell-membrane mediated, 114
 characteristics of, 140–141, 381
 cholesterol in, 118–119, 392
 enhancement of, 115–116, 353
 fatty-acid composition and, 113–116, 121
 haptens and, *see* Haptens
 in vivo versus *in vitro* approaches in, 121–122
 lateral distribution of antigens/haptens in, 124–128, 135, 137
 phase separation in, 121
 phase transition temperature and, 117–118
 phospholipids in, 112–119, 353, 392–394, 427
 research consideration in, 111, 116, 120–121, 429
 spin-membrane immunoassay (SMIA) in, 139–148
- Immune RNA (IRNA):
 liposomes containing, preparation of, 308–309
 in lymphocyte activation, 318
- Immunoassay techniques, 139–146
- Immunoglobulin (IgG):
 in complement fixation, 126–129
 in endocytosis stimulation, 237–238
 in liposome uptake facilitation, 237–240, 317–318, 357
 in lymphocyte activation, 317–318
 in monocyte-mediated erythrocyte lysis, 132–134
 as targeting antibodies, 317, 318
- Interconversion rate, of liquid-gel transition, 27
- Influenza virus, 276
- Intensity ratios, 68–69
- Insulin therapy:
 liposomes as carriers in, 292–298, 354
 by oral administration, 292–298

Interferon, 309, 312-317

Intrinsic viscosity, 35, 40-41

Ionic charges, *see* Surface charges

Isotopic labeling:

of actinomycin D, 326-328

in IgG-coated liposome uptake, 240-244

of cytosine arabinoside, 375

in liposome-cell membrane interactions, 164-165, 182-183, 202

in lymphocyte activation, 318

in lysosomotropic uptake, 230

of methotrexate, free and encapsulated, 396-400

multiple detection of, 141-144

in phospholipid molecule exchange, 150

in specific tissue uptake studies, 299

spin labels as, 139-144

in tissue distribution studies, 326-328

of thyroid-stimulating hormone (TSH), 299

of tumor-therapy carrier liposomes, 286

in tumor-tissue localization, 298, 352

Kupffer cells, liposome uptake by, 230, 232, 240, 345

Large unilamellar vesicles (LUVs):

cocleated cylinders in, 260

encapsulated volume and efficiency of, 264

poliovirus encapsulation by, 268-274

preparation of, 259-260, 374

properties of, 260-265

terminology for, 367, 368

tissue uptake of, 375

toxicity with, 376

Lateral mobility:

complement and, 126-128, 135, 137

constants for, of spin-labeled phospholipids 126

Lateral phase separation, 178, 212

Leakage:

from carrier liposomes, 176, 228-229, 349, 402-406, 414

cholesterol and, 402-404

of cytotoxic drugs, 349

of lysosomotropic drugs, 228, 229

secondary carrier role in, 349

tissue distribution problem and, 350

as tumor-therapy strategem, 290

of vesicle into cytoplasm, 176

Lecithin, *see* Phosphatidylcholine (PC)
egg, *see* Egg phosphatidylcholine

Leukocytes:

actinomycin D effects on, 328-329, 331

liposome uptake by, 240-244, 284

Lipid(s), *see also* Lipid bilayer(s); Liposomes; Phospholipids

crystallization of, and protein aggregation, 75

fluidity of, 67; *see also* Membrane fluidity

incorporation into intact cells, 215-217

in liposome immunity enhancement, 116, 123

liquid-gel molecular transitions of, *see* Phase transition(s)

membranes, *see* Lipid bilayer(s)

molecular conformations of, 9-19

polypeptides and, *see* Polypeptide-lipid systems

Lipid bilayer fusion, *see also* Cell fusion; Liposome-cell membrane interaction

calcium ion induction of, 50-56, 61, 65, 175-178, 182, 260-267

domain size and, 64-65

ionic surface charges and, 61

magnesium ion induction of, 50, 53-56, 61

of mixed phospholipids

Lipid bilayer ratio (X), 40-44

Lipid bilayer packing geometry, *see* Packing geometry, lipid molecule

Lipid bilayer vesicles, *see also* Liposomes
asymmetry of, 29, 44-46

barrier functions of, 85-93

biological membranes and, 2-4, 85;
see also Model membrane systems

bound water of, 38-39

characteristics of, 9-16

cholesterol effects on, 73-74, 77-79, 94-96

of egg PC, *see* Egg phosphatidylcholine
electrostatic charges on, *see* Surface ionic charges

encapsulated volume of, 264

geometric packing of, *see* Packing geometry, lipid molecule

gramicidin A spanning of, 68

head-group area calculations, 46-47

heterogeneity parameter (p) of, 33-34

hydration of, calculations, 38-40

hydrodynamic analysis of, 29-49

intrinsic viscosity analysis, 35, 40

ionotropic phase transitions in, 50

large, *see* Large unilamellar vesicles (LUV)

- Lipid bilayer vesicles—Continued
 liquid-gel transitions in, *see* Phase transition(s)
 local anesthetics and, *see* Local anesthetics
 model membrane characteristics of, *see* Model membrane systems
 molecular number, calculations, 38, 41
 molecular volume in, 44–46
 multilamellar, *see* Multilamellar vesicles (MLV)
 nitroxide spin-label sensitized, 124
 outer to inner layer ratio, 40
 permeability in, *see* Permeability, lipid bilayer
 phase separation, in mixed, 56–57
 -lateral, 178, 212
 phase transitions in, *see* Phase transition(s); Phase transition temperature
 preparation of, *see* Liposome preparation
 sedimentation coefficient, 32
 shape of, calculation, 38
 small, *see* Small unilamellar vesicles
 surface charges on, *see* Surface charges
 thermotropic phase transitions of, 50;
 see also Phase transitions
 thickness of, 44–47
 transport process in, 32
 trapped water in, 36–37
 water in, 36–41
- Lipid bilayer fusion, *see also* Liposome-cell membrane interaction
 calcium ion induction of, 50–56, 61, 65, 175–176, 178, 182, 260–267
 domain size and, 64–65
 magnesium ion induction of, 50, 53–56, 61
 of mixed phospholipids, 56–57, 60, 160–161
 surface charge asymmetry and, 61
- Lipid bilayer ratio (X), 40–44
- Lipid molecule packing geometry:
 asymmetries of monolayers in, 43–47
 of egg phosphatidylcholine vesicles, 29, 43–46
 of lipid bilayer vesicles, 43–46
 in polypeptide-lipid systems, 73
- Lipid molecules, *see* Phospholipids
- Lipid-water dispersion systems:
 phase transition enthalpy in, 70–73
 polypeptide concentrations and, 72–73
- Liposome(s), *see also* Lipid bilayer vesicles; Phospholipids
 actinomycin D encapsulation in, 325–339
 aerosolized, 418
 anesthetics and, 101, 109; *see also* Local anesthetics
 animal experiment model of, 426–431
 antibodies and, 115, 140–141
 antigens and, *see* Antigens
 in antitumor chemotherapy, *see* Antitumor chemotherapy
 aqueous phase (APL), 326–339
 as biodegradable, in lysosomes, 231, 233
 blood-brain barrier problem, 284
 calcium ion effects on, *see* Calcium ions
 catabolic degradation of, 314–317
 cell membrane interactions with, *see* Liposome-cell membrane interactions
 characterization and properties of, 1, 5, 140, 343–346, 367–369, 387
 cholesterol effects on, *see* Cholesterol in circulatory system administration, 416–417
 cytotoxic effects of, *see* Cytotoxicity
 development in concepts and uses of, 2–7, 29, 50, 85, 111, 281, 343–349, 426–431
 in diagnostic antibody production, 115
 DNA role in, *see* Deoxyribonucleic acid (DNA)
 in drug administration, 259, 281, 344–346, 355–357, 376–378, 404–405, 431–432; *see also specific drugs by name*
 efficiency and size of, 357
 empty, 402
 encapsulation of drug agents by, 259, 325–329, 402–406, 412–419; *see also* Antitumor chemotherapy; Encapsulation, and specific substances by name
 endocytosis of, *see* Endocytosis
 entrapment of, by tissues and organs, *see* Tissue uptake
 as enzyme carriers, 235–245
 in enzyme replacement therapy, 235–236, 346–349
 erythrocytes as, 367
 functional-environmental potentials, 355–357
 fusion of aggregates of, *see* Lipid bilayer fusion
 fusion with cells, *see* Liposome-cell membrane fusion

Liposome(s)—Continued

as host cells, in viral interactions, 278–280

human clinical applications of, 350–361, 365, 426–431; *see also* Antitumor chemotherapy

immune response of, *see* Immune response

immunoglobulins and, 237–245, 317–318, 357

immunologic potentials of, 111–119, 123, 353–354, 432

insulin therapy via, 292–298, 354

in interferon synthesis, 313–314

in vivo administration of, 239–245, 406–412, 426–429

ionic charges on, *see* Surface charges
large, *see* Large unilamellar vesicles (LUV)

leakages from, *see* Leakages

lipid phase (LPL), 326–339

in lymph node localization, 290–292

lymphocyte activation via, 317–319

lysosomal uptake and degradation of, 230–231, 233

in lysosome storage disease, 346–349
as lysosomotropic carriers, 226–230

as macromolecule carriers, *in vivo*, 265
methotrexate (MTX) containing, 395–410; *see also* Methotrexate

in model membrane systems, *see* Model membrane systems

monocytes and, 129–133

multilamellar, *see* Multilamellar vesicles (MLV)

nomenclature for, 367–369

phase separations in, *see* Lipid bilayer vesicles

phospholipid molecule exchange in, 150–156, 160–163

phospholipids in, *see* Phospholipids, *and specific types by name*

in polioviral transmission, 269–275

polyribonucleotides encapsulated in, 308–324; *see also* Polyribonucleotides

preparation of, *see* Liposome preparation

proteolysis inhibition by, 292–299

purity criteria problem, 370

release of encapsulated materials from, 176–177, 419–424

in respiratory distress therapy, 418–425

second carrier developments in, 349

size and sizing of, 253–255, 257–259, 286, 352, 368, 397, 399, 400, 412

sonication of, *see* Sonication

surface charges on, *see* Surface charges
sustained release of drugs from, *see* Sustained time release

targeting of, *see* Targeting

terminology for, 367–368

therapeutic applications for, 281–282, 298–302, 306–307, 343–370, 426–431; *see also* Antitumor therapy

tissue-specific localization with, 284, 299–300, 306–307, 349–350, 353; *see also* Tissue uptake

toxicity of, *see* Cytotoxicity

tumor-cell uptake monitoring of, 286–290

type specificity of, 250

uptake of, by organs and tissues, *see* Tissue uptake

vesicle characteristics and entrapped drug availability, 431–432

viral receptors in, 275–277

volume trapping by, 36–38, 253–254, 257

viruses and, *see* Viruses

Liposome-cell membrane interactions, 218
adhesion in, 187–194

adsorption in, 166, 169, 171, 175, 182, 276

agglutination in, 201

apparent fusion index (AFI) of, 205
asymmetrical vesicles in, 194–196

binding in, 166*n*, 173, 275–277

calcium ion induction of, 61, 65, 175–182, 216–219

capping in, 173–174

cell-line genetic factors in, 248

cell plasma role in, 165–166, 171–172, 178–179, 395

cell proliferation and, 198

cell type differences and, 182–183

chemical factors effecting, 195, 200–204, 216–217, 238–239

cholesterol in, 195, 277, 405

egg phosphatidylcholine and, 167–168

electronmicroscopic evidence of, 171, 172

endocytosis and, 164–170, 176–178, 230

erythrocytes and, 201–214

exchange proteins in, 192–195

exocytosis and, 61, 230–231

freeze-fracture evidence of, 172

glycoproteins in, 420

hydrophobic protein transfer in, 174

interferon induction by poly(I): poly(C) in, 312–313

in vivo mechanisms of, 405–406

lipid degradation and, 198

Liposome-cell membrane interactions—

Continued

- lipid-membrane component exchanges in, 166, 170, 238
- lysophosphatidylcholine in, 175–176, 201, 238–239, 248
- mammalian cells in, 185–199
- methods of study of, 164–165, 200
- mechanisms indicated for, 165–166, 200–201, 218, 395, 405–406
- metabolic inhibitor effects in, 186–187
- net transfer in, 149, 195, 218
- phase transition temperature and, 168–170, 187–192
- polyribonucleotide (poly[I]:poly[C]) in, 313
- reciprocal component transfer in, 166*n*, 170
- release of encapsulated materials in, 165, 173, 176–177, 216–217
- in *Salmonella*, 215–225
- surface ionic charges in, 167–168, 175, 238–239, 249, 312
- targeting as, *see* Targeting
- temperature and uptake in, 238–239
- tissue uptake as, *see* Tissue uptake
- transfer as, 218
- vesicle properties and, 178
- by viral infection, 275–278

Liposome preparation:

- actinomycin D containing, 326
- asymmetric vesicles, 194–195
- cytosine arabinoside (ara-C) entrapped, 373–374, 388
- cytosine triphosphate arabinoside (ara-CTP) entrapped, 373–374
- egg phosphatidylcholine, 29–30, 185
- by ether injection, 250–258
- ionic strength and, 258
- multilamellar, 373
- methotrexate (MTX) containing, 397–399
- negatively charged, 373–374
- multilamellar-IRNA, 308
- positively charged, 373–374
- spherical, 265
- SUV-*Salmonella*, 215
- ultrasonically irradiated, 30
- unilamellar, 250–256
- viral infected, 276

Lipopolysaccharides, 111

- translocation of, in *Salmonella*, 221–222, 225
- in vesicle transfer activity, 217

Liquid crystalline-gel transitions, *see* Phase transitions

Local anesthetics:

- capping inhibition by, 174
- concentration and lipid interactions in, 27–28
- egg PC interactions with, 20, 21
- membrane permeability and, 19
- phospholipid membrane binding to, 20–22

Lymph node localization, 290–292

Lymphocytes:

- actinomycin D effects on, 336–337
- antibody-phospholipid formations and, 116
- LUV-cell absorption in, 187, 189
- liposome content interaction sites for, 423
- tumor-cell toxicity activation and, 317–320

Lysolecithin, *see* Lysophosphatidylcholine (LPC)

Lysophosphatidylcholine (LPC), in liposome-induced cell fusion, 175–176, 201, 238–239, 248

Lysosomal storage disorder, 346–349

Lysosomes:

- carrier liposome uptake and, 345–346
- endocytic vacuoles and, 177
- enzymatic genetic disorders and, 235
- in lipid vesicle uptake, 165, 176–177
- in lysosomotropic carriers, 226–227, 234

Lysosomotropic carriers:

- active agents carried by, 226–229
- characteristics of, 226–227
- endocytosis of, 226, 227, 230
- extracellular release of, 228, 234
- ionic charges in, 232–233
- liposomes as, 226–234
- target accessibility in, 229–230

Lysozymes, 236, 240, 244

Macroglobulin (IgM), in complement activation, 128–129, 428

Macromolecules, encapsulation of, 259–267

Macrophages:

- in actinomycin D-liposome uptake, 338
- liposome uptake by, 240

Magnesium ion(s):

- in binding with PS, 57–59
- in membrane fusion, 50–51
- in phase transition temperature changes, 50–53, 90
- in phospholipid vesicle fusion, 53–56
- in vesicle lipid incorporation by cells, 216

- Markers, isotopic, *see* Isotopic labeling
- Mammalian cells, phospholipid interactions with, 185-199
- Melphalen, 349
- Membrane(s):
- asymmetry of, *see* Asymmetric membranes
 - biological, *see* Biological membranes
 - fluidity of, 167, 175, 238
 - fusion of, *see* Cell fusion; Lipid bilayer fusion; Liposome-cell membrane interaction
 - immunoassay of, 139-148
 - microsomal, 153-156
 - mitochondrial, 175
 - surface charges on, *see* Surface ionic charges
- Metabolic inhibition, 186-187, 427
- Methotrexate (MTX):
- in carrier liposomes, 349
 - clearance, of free and entrapped, 396-401
 - metabolism of,
 - compared with cytosine arabinoside, 406
 - species variance in, 409
 - plasma level maintenance of, 404-405
 - surface ionic charges and entrapment of, 396
 - therapeutic effectiveness of, 401-410
 - toxicity of, 402-403
 - tumor cell response to, 402-404, 427
- Micrococcus freudenreichii*, 15-16
- Micropinocytosis, 169
- Microsomal phospholipids, 153-156
- Mithramycin, 238
- Mitochondrial membranes, 75
- MLV, *see* Multilamellar vesicles
- Mobility, molecular, 11-14, 28
- Model membrane systems:
- biological membrane convergencies with, 5, 9-16, 67, 85, 185
 - historical development in, 2-5
 - in immunology, 111-112, 124-138
 - lipid bilayers as, 29, 60, 85, 124
 - liposomes as, 3, 200, 281
 - of lipid phase transitions, 8, 50
 - local anesthetics in, 19
 - therapeutic dimensions for, 343-346
- Molecular number, 38, 41
- Molecular phase transitions, *see* Phase transition(s)
- Molecular segmental order:
- cholesterol and, 17-19
 - in egg phosphatidylcholine, 16-17
 - local anesthetics and, 19
 - mobility and, 12, 28
 - water exclusion by, 28
- Monocytes, 129-133
- Monolayers, 43-47
- Monovalent cations, 88
- M protein, 279, 280
- Multilamellar vesicles (MLV):
- drug delivery by, 259, 377
 - encapsulated volume and efficiency of, 264
 - fusion with plasma membrane, 165, 171, 237
 - polyribonucleotide entrapment in, 308-310
 - preparation of, 373
 - tissue uptake of, 310, 375, 412-413
- Mycobacterium bovis* (BCG), 430-431
- Mycobacterium tuberculosis*, 353
- N**egative charges, *see* Surface ionic charges
- Negative stain, in sizing liposomes, 253-255
- Net transfer, in liposome-cell membrane interactions, 149, 195, 218
- Neuraminidase, 345-347
- Nomenclature, for liposomes, 367-369
- Nuclear magnetic resonance (nmr), 8-24, 40-43, 157
- Nucleic acid, liposome encapsulation of, 308-324; *see also* Polyribonucleotide
- Neutrophilic granulocytosis, 337
- O**lefins, 76-77
- Oleic acid, 11
- Order parameter, *see* Molecular segmental order
- Osmotic shrinkage, 94
- Osmotic stress, 214
- Oxidation, and aging, 83
- P**acking geometry, lipid molecule:
- asymmetry of, 46; *see also* Asymmetric membranes
 - of bilayer vesicles, 29, 43-47
 - of biological membranes, 157-158
 - characterization of, 29, 46
 - of egg phosphatidylcholine vesicles, 29, 43-46
 - in polypeptide-lipid systems, 73
 - of proteins, 73-74
 - quantitative analysis of, 43-45
 - random arrays, 73-74

- Palmitic acid, 22-23
Paramagnetic resonance spectra (pmr),
124
Paramyxovirus, 275-277
Parenchymal cells, carrier liposome up-
take by, 345, 434
Partial specific volume, 35-36, 44
Partition coefficients (K), calculation of,
103-105
PC, *see* Phosphatidylcholine
PE, *see* Phosphatidylethanolamine
Permeability, lipid bilayer:
alkane chain length and, 88
ion size and, 88
monovalent cations and, 87, 88, 90
temperature and, 86-88, 92
of water-contained, 86-87, 94, 100
Phagocytosis:
conditions affecting, 238-239
enzyme uptake in, 237-238
of erythrocytes, 130
Phagolysosomes, 230
Phagosomes, 230-231
pH:
in cell fusion, 209-212
in local anesthetic-lipid interactions, 20,
21
Phase transitions, liquid-gel:
in *Acholeplasma laidlawii*, 24
bilayer barrier functions and, 85-89, 93
in biological membranes, 50, 75-76
bivalent cation effects on, 50-59
cholesterol and, 77-78, 94
enthalpy of, 70-72, 74
ionic charges in, 51-53
membrane fusion and, 60-61
in mitochondrial membranes, 75
permeability and, 86-88, 92
in polypeptide-lipid systems, 69-72
temperature in, *see* Phase transition
temperature
Phase transition temperature (T_c):
in biological membranes, 50-51, 85-86
bivalent metallic ions and, 51-53, 56, 90
bond saturation and, 84
carrier liposomes and, 354, 381
cell growth temperature and, 87
in channel formation, 68
lipid bilayer properties and, 86-87
in liposome-cell membrane interaction,
168-170, 189-192
in liposome immunity response, 118
in membrane fusion, 60-61
monovalent cation permeability and, 88
negative ion charge neutralization and,
51
in partition coefficient calculations,
103, 104
protein aggregation and, 75
water permeability and, 86, 100
Phosphatidylcholine (PC), *see also* Phos-
pholipids
asymmetric vesicles, preparation of,
194-195
egg PC, *see* Egg phosphatidylcholine
in cell fusion, 201
in cholesterol affinity series, 96-97, 100
local anesthesia interactions with, 20,
21
phase transition temperature and fusion
in, 53, 168-169
in phospholipid exchange protein stud-
ies, 149-158
vesicle transfer inactivity of, 217
in viral-liposome fusion, 277
Phosphatidylethanolamine (PE):
in cholesterol affinity series, 97
dinitrophenyl (DNP) derivatives in
immune reactions, 111-119
N-substituted derivatives, of, in immune
reactions, 114-119
in phospholipid exchange protein stud-
ies, 149-158
in virus-liposome fusion, 277
Phosphatidylinisol (PI), 149-158
Phosphatidylserine (PS):
binding of, with Ca^+ and Mg^+ ions, 57,
63-64
calcium ion effects on, 52-54, 58, 59
exchange protein transfer in, 150
isothermic phase transitions in, 53-55
local anesthesia interactions with, 20,
21
magnesium ion effects on, 57-64
membrane thickness changes in, 59
phase transitions in, 53-55, 59
Phosphatidylstearylamine liposomes, 201,
209-212
Phospholipases, in biomembrane transfer
and asymmetry, 157-158
Phospholipid(s), *see also* Lipids; Lipid
bilayer vesicles; Liposomes
in antibody response enhancement, 338
in blood-clotting, 4
cell membrane transfer of, 218-223
cell release of adsorbed, 189-194
cholesterol and, *see* Cholesterol
as drug carriers, 345, 354-361
egg PC as, *see* Egg phosphatidylcholine
exchange of, vesicle to cell, 149, 150,
170; *see also* Phospholipid ex-
change protein

- Phospholipid(s)**—Continued
 immunogenic effectiveness of, 117–118, 392–394
 local anesthesia and, 19–22, 101–104
 microsomal, 153–153, 156
 as model systems, *see* Model membrane systems
 in partition coefficient measurement, 103–104
 in respiratory distress therapy, 418
 therapeutic applications of, *see* Antitumor chemotherapy
 toxicity of, *see* Cytotoxicity
 in viral membrane-liposome fusion, 277
Phospholipid exchange proteins, *see* Exchange proteins, phospholipid
Picornaviruses, 268–274
Plaque-forming cells (PFC), 116
Plasmalogens, 3, 83
Polar drugs, encapsulation of, 412–415
Poliioviruses, 269–274
Poly(I):poly(C), *see* Polyribonucleotides
Polyamino acids, 406
Polypeptides, *see also* Proteins
 coordination number of, 73
 lipids and, *see* Polypeptide-lipid systems
 liposome-encapsulation of, 264–265
 in mixed, lipid-water systems, 72–73
Polypeptide-lipid systems, 68–75
 biological membrane implications of, 73–75
 component arrangements in, 70
 phase transitions in, 69–72
 random arrays in, 73
Polyribonucleotides (poly[I]:poly[C]):
 in antiviral resistance, 331–312
 carrier liposome entrapment by, 308–311
 cytotoxicity of, 313
 in interferon synthesis, 312–314
 in lymphocyte activation, 317–318
 protection of, from catabolic degradation, 314–317
Polyvinylpyrrolidone, 354
Pompe's disease, *see* Glycogen storage disease
Positively charged liposomes, *see* Surface ionic charges
Potassium ions:
 cholesterol effects on, 94–96
 permeation by, 88, 90, 94–96, 101, 102
 valinomycin and, 3, 94–96
Procaine, 19–21; *see also* Local anesthesia
Proteins, *see also* Polypeptides
 in adsorption and targeting, 406
 aggregation of, 75
 in biological membranes, 67–68, 75
 boundary layer effects with, 72
 cardiolipin and, 150
 exchange, *see* Exchange proteins, phospholipid
 lipid bilayer spanning by, 67–68
 in lipid bilayer systems, *see* Polypeptide-lipid systems
 in paramyxovirus membrane, 275
 random arrays of, 73–74
 in viral-liposome fusion, 278–279, 280
- Q**uadrupole splittings, in phospholipid membranes, 20–28
- R**adioactive labeling, *see* Isotopic labeling
 Random arrays, 73–74; *see also* Packing geometry
 Reciprocal component transfer, 166*n*, 170
 Red cell ghosts, *see* Erythrocyte ghosts
 Relaxation time, 10–11
 Respiration, endocytosis and, 168
 Respiratory distress syndrome (RDS), 418
 Respiratory system, liposomal therapy for, 418–425
Reticuloendothelial system:
 actinomycin D uptake by, 326–331
 -toxicity effect of, 335–339
 carrier liposome uptake by, 284, 288–289, 291, 315–317, 345, 349, 357, 428
 drug administration via, 430
 MTX uptake by, 399–400, 405
Ribonucleic acid (RNA):
 immune, 308, 318
 messenger, 433
 polioviral, 270–273
 viral, encapsulation of, 368
 -in liposome fusion, 277–278
- Salmonella**, 215, 225
 lipid vesicle incorporation by, 215, 216–219
 membrane composition differences in, 224
 translocation of lipids, intracellular, 219
 Second carrier, liposomal, 349
 Sedimentation coefficient, 32, 36
 Segmental order, *see* Molecular segmental order

- Sendai virus, 276-278
 Sensitizer, 139-140
 Shrinkage velocity, 86
 Simha coefficient, 40
 Sindbis virus, 276
 Small unilamellar vesicles (SUV):
 cell fusion induction by, 175
 drug carrier potentials of, 259
 in cytosine arabinoside (ara-C) delivery, 374
 in cytosine triphosphate arabinoside (ara-CTP) delivery, 376, 377
 encapsulated volume of, 264
 stability of, 257-258, 370
 sonicated, 368
 surface ionic charges on, 175, 414;
 see also Surface ionic charges
 tissue uptake of, 375, 381, 412, 413
 Sonication:
 carrier liposome uptake and, 397-404, 410
 in cell fusion, 209, 250, 410
 in clearance of MTX, 397, 399, 400
 release from encapsulation by, 415
 standardization for, 370
 therapeutic efficiency and, 399-402
 Spectrin-actin complex, 90, 99, 100
 Sphingomyelin:
 antienzymatic stability of, 391
 beef, 117-118
 in cholesterol affinity series, 97
 exchangeability of, 154
 Spin-membrane immunoassay (SMIA), 139-148
 Spin labels, *see* Isotopic labeling
 Spin-lattice relaxation time, 10
 Spin-spin relaxation time, 10
 Spleen, *see* Reticuloendothelial system
 Statolon, 314
 Stearic acid, 20, 21
 Stearylamine (SA):
 in agglutination, 201
 in cell fusion, 201, 212
Streptomyces hydrogenans, 87
 Surface ionic charges:
 in antigen enhancement, 353, 366
 asymmetry of, in membrane fusion, 61
 in cell-to-cell fusion, 175
 clearance rate and, 412
 in cytosine triphosphate-arabinoside (ara-CTP) entrapment, 374, 375
 cytotoxicity and, 285, 376, 378, 381, 392
 in DNA synthesis inhibition, 375-377
 in drug encapsulation, 265, 310-311, 315-317, 392, 396, 413-414
 in drug uptake, 349-350, 406, 412
 in endocytosis, 238, 412
 in enzyme-bearing liposomes, 237, 285
 in ganglioside receptors, 276
 in leukopenia, 243-244
 in liposome-cell membrane interaction, 60, 167-168, 175, 238-239, 249, 312
 in lymph node localization, 290-291
 in lymphocyte activation, 320
 methotrexate entrapment and, 396
 in polyribonucleic acid entrapment, 310-311, 315-317
 in spleen-enhanced liposome uptake, 291
 in subcellular localization, 232-233
 in SUV sustained release, 414
 in toxicity, *see* Cytotoxicity
 in viral resistance by cells, 331
 Surfactant replacement, by liposomes, 418-419
 Sustained time release:
 of cytosine arabinoside (ara-C), 371, 385-386, 390-391
 encapsulation and, 386
 endocytosis and, 386
 intermittent versus, 380-383, 390-391, 409, 429-430
 liposome carriers for, 371, 380-381, 385-386, 390-391, 429-430
 massive dosage versus, 429-430
 of methotrexate, 409
 by positive SUVs, 414
 SUV, *see* Small unilamellar vesicles
 Symposium on Biophysics and Physiology of Biological Transport (1965), 5
- T**argeting:
 actinomycin D in, 320-321
 cell proliferation and, 431
 characterization of, 419-420
 of drug carrier liposomes, 284, 317-321, 349-350, 354-355, 406, 420;
 see also Tissue uptake
 of enzymes, 235-245
in vivo problems of, 284, 406-407, 426, 429
 in liposome-cell membrane interaction, 420
 protein adsorption in, 406
 Tay Sachs disease, 235-245, 284
 T-cell, *see* Lymphocytes
 Temperature:
 in lipid vesicle phase transition, *see* Phase transition temperature

- Temperature—Continued
 in paramyxovirus-liposome fusion, 280
 in vesicle-cell lipid uptake, 238–239
- Tetracaine (TTC), 19–21
- Therapy, *see* Antitumor therapy; Respiratory system
- Thermotropic phase transition, 50, 53;
 see also Phase transition temperature
- Thyroid stimulating hormone (TSH), 299
- Tilorone, 314
- Time-spaced release, *see* Sustained time release
- Tissue uptake:
 of actinomycin D, 326–329
 of cholesterol, 396–402, 405, 406
 criteria for distribution in, 350
 of cytosine arabinoside, 375–378
 of drug carrier liposomes, 284, 317–321, 349–350, 354–357, 399–406, 416–417; *see also* specific drugs by name
 of large unilamellar vesicles, 375
 by liposome size, 375, 412, 413
 by liver, 284, 288–289, 299, 315–317
 metabolic inhibitor effects on, 186
 of methotrexate, 399–407
 of multilamellar vesicles, 410
 by organ systems, 412–413
 of small unilamellar vesicles, 375, 412–413
 by specific tissues, 299–300, 306–307, 317–321, 353–357, 419–420
 by spleen, 284, 288–289, 299, 315–317
 surface ionic charge and, 349–350, 412
 targeting of, 406; *see also* Targeting tumors and, *see* Tumors
- Transfer:
 definition of, 218; *see also* Liposome-cell membrane interaction
 exchange as, 149, 160–161; *see also* Exchange protein, phospholipid
 of membrane proteins, 225
 net, 149, 195, 218
 of phospholipids, between cell membranes, 219–223
 of saccharides, 221, 222
- Translocation, *see* Transfer
- Transport process, hydrodynamic, 32
- Trapped volume, *see* Volume trapping
- Tritium, *see* Isotopic labeling
- Trypsin, in phospholipid release, 189–193
- Tubocurarine, 354
- Tumors:
 antigen specificity for, 429
 chemotherapy for, *see* Antitumor chemotherapy
 drug carrier liposome uptake by, 352, 266
 localization of, 286–290
 lymphocyte activation against, 317–320
 methotrexate and, 402–404, 427
 radioactivity uptake by, 285–390, 352
- Ultracentrifugation, 32–36
- Ultrasonic irradiation, 30
- Unilamellar lipid vesicles, *see* Large unilamellar vesicles; Lipids; Small unilamellar vesicles
- Valinomycin, K ion leakage and, 94–96
- Vesicles, lipid, *see* Lipids; Lipid bilayer vesicles; Liposomes
- Vesicle hydration water, 38
- Vesicle molecular number, 38, 41
- Vesicle-trapped volume, 36–40; *see also* Volume trapping efficiency
- Vinblastine, 337, 412, 414
- Viral receptors, 275–277
- Viral RNA:
 encapsulation of, 270–271, 368
 in liposome fusion, 277–278
- Virosomes, 300, 353
- Virus(es), *see also* Paramyxovirus; Poliovirus, and other specific types by name
 endocytosis of, 177
 liposome interactions with, 300
 resistance to, 311–314
- Viscosity, intrinsic vesicle, 35, 40, 41
- Volume-trapping efficiency, of liposomes
 alcohol injection method, 257
 aqueous concentration and, 266–267
 calcium-induced, sonicated, 264
 ether injection made, 252–256
 handshaken (Babraham method), 257
 by size and type, 259, 264
- Water, phospholipid
 bound, in liposomes, 38–40
 of hydrated, calculation of, 39–41
 permeability of, *see* Water permeability trapped, 36–37
- Water permeability, phospholipid
 cholesterol effects on, 94
 phase transition temperature and, 86–87, 100
- White blood cells (WBC), *see* Leukocytes





Index of Contributors

(Italicized page numbers refer to comments made in discussion.)

Allen, N., 70-96, 95-96

Bachrach, S., 374, 393, 438

Bateman, J. L., 390-391

Bennett, D. B., 110-120, 141-142

Beresford, H. R., 339-348, 345-348, 392-393, 433-434, 436, 437, 438, 439, 440

Boshes, B., 11-18, 225-226, 328, 347

Braunstein, P., 143-167, 168-183, 211, 214, 263, 265-271, 280

Brun, A., 184-214

Brush, J., 398-416

Burkholder, J., 70-96

Capron, A. M., 45-61, 347, 349-362, 359-362, 373, 390, 391-392

Caronna, J., 95, 264

Carse, J. P., 322-328, 327, 328

Chaloner, J., 281-292

Comiscioni, J., 70-96

Cranford, R. E., 440-441

Fein, J., 97-104, 108, 208, 418-419
Frappier, J., 345

Gayet, H., 241-251

George, A. E., 168-183

Glass, 96

Goldensohn, E. S., 137-142, 140, 141, 209

Goldman, M. H., 141, 263, 438

Goodman, J., 211-214, 259-261, 280

Grenvik, A., 96, 141, 226, 227, 346, 437

Harden, A., 281-292

Hardy, P. M., 393

Hass, W. K., 105-109, 108, 109, 214

Hauerwas, S., 329-338, 337-338

Hawkins, R. A., 105-109

Henry, C., 337

Hinterbuchner, L. P., 140

Horan, D. J., 363-375, 373-375, 393

Hughes, J. R., 121-136, 140-141, 279

Ingvar, D., 96, 108, 109, 184-214, 208-209, 210, 211, 214, 224, 304

Johansson, L., 184-214

Kalkines, G., 425-431

Keene, B., 347, 376-393, 391, 392, 393

Kleiman, M. A., 425-431

Knill-Jones, R. P., 293-306

Korein, J., 1-5, 6-10, 19-38, 95, 96, 142, 143-167, 168-183, 256-259, 265-271, 320-321, 439-440

Kricheff, I. I., 143-167, 168-183

Leaffer, T., 318, 359, 360

Levy, D. E., 293-306, 304-305

Lieberman, A., 143-167

Milhaud, A., 241-251, 263-264, 434-436

Molinari, G. F., 62-69, 96, 210, 279, 280, 305

Moraczewski, A. S., 318, 327

Nathanson, M., 209-210

Nesbakken, R., 319, 320, 348, 439

O'Brien, J., 281-292

Ouaknine, G. E., 252-264

Pampiglione, G., 141, 210-211, 280, 281-292, 291, 305

Pearson, J., 108-109, 214, 265-271, 279-280

Pinto, R. S., 168-183, 208

Plum, F., 224-225, 226-227, 261-262, 263, 280, 291-292, 293-306, 305-306

Posner, J. B., 215-227, 226

Riboulot, M., 241-251

Roelofs, R., 39-44

Samuelsson, S. M., 184-214

Satran, R., 108

Suter, C. R., 142, 262, 291, 398-416, 437, 439

Tendler, M. D., 394-397, 420-422

Van Till, A., 96, 346, 361, 373, 374, 439

Veatch, R. M., 307-321, 318-320, 327-328, 337, 338, 419-420, 422-423

Veith, F. J., 417-441, 434, 436, 438, 439, 440

Vernon, S., 347, 392

Walker, A. E., 228-240, 263, 264, 272-280, 305

Woolsey, R. M., 361

Youngstein, K., 391

Zimmet, J., 436-437

Subject Index

- A**bdominal reflexes as criteria in brain death, 71, 84, 85
- Akinetic mutism, 203, 219–221, 225
- Alaska, 1974 statute in, 429
- Alpha coma, 219, 408, 409, EEG of, 131
- Altered consciousness, anatomy of, 221
- American Bar Association, statute proposed by, 354, 365–367, 430–431
- Angiography
carotid and vertebral, 253
and changes in status of CBF, 208
in demonstrating CBF, 211, 231
in diagnosing brain death, 31, 231, 238
gamma imaging technique, 211–214
See also Intracranial angiography
- Ankle reflexes as criteria of brain death, 71, 85, 86
- Anoxia
in cats, 231
EEG in, 284, 286–287, 289
effect on brain, 97–98
- Apallic syndrome, 21, 219, 302
case material on, 186–198
CBF in, 184, 202, 204–205
corneal reflex in, 201
definition of, 9, 184–185, 202–203
EEG in, 184, 202–203, 205
eye movement in, 304
pathogenesis, 203–204
pupillary reflex in, 201
spinal reflexes in, 201
term discussed, 225
- Apnea
correlations with ECS, 114, 116
defined, 9, 113
diagnosis in comatose patients, 216–217
in disconnecting tests, 241–250
and patients with brain waves, 117–119
quantification of, 241
- Apneic oxygenation, technique of, 217
- Arkansas, 1977 right-to-die law in, 52
- Artifact
in CT scans, 403
muscle, in EEG, 406–408
- Arteriovenous oxygen difference (AVDO₂)
in cerebral metabolism, 228–229
in determining brain death, 238
- Artificial respiration, effect on brain, 275
- Astrocytes, in defectively perfused brains, 270
- Atropine test, 253–255
- Audio-ocular reflex
as criteria in brain death, 71, 74, 75, 83, 85, 91
with cardiac arrest, 88
in normal subjects, 87
- Auditory blink reflex, *see* Audio-ocular reflex
- Autolysis, with absent bolus, 267
- AVDO₂, *see* Arteriovenous oxygen difference
- B**arbiturate intoxication
AVDO₂ in, 230
brain death and, 141
in disconnecting test, 241
ECS and, 122–123
- Biblical law, brain death and, 394–395
- Biceps reflexes as brain death criteria, 71, 85
- Black's Law Dictionary*, definition of death in, 345, 425–426
- Blood flow, cerebral, *see* Cerebral blood flow
- Bodily integration, and definition of death, 310–312, 314, 315
- Body, Christian view of, 332
- Body fluids, and definition of death, 310, 314, 315
- Bolus technique, 162, 211, 253
advantages and limitations, 238
angiography and, 169, 178
clear head bolus in, 149, 150, 152–153
in evaluating cerebral circulation, 143–163, 231
in infants and children, 163
“intermediate” head bolus, 153–164, 161–162, 168
return of flow in, 280
“small” head bolus in, 155–156, 162, 168
technique for, 145–148
- Brain
as control system, 24–25
diencephalon, 273
electrical activity of, 234–236
observation, with bolus technique, 267–271
regional glucose metabolism, 106

Brain—(cont'd)

- weight of, 279–280
- See also*, Cerebellum; Cortex; Critical system
- Brain autopsy in brain death, 253
- Brain death
 - apallic syndrome vs., 202–203
 - Biblical law and, 394–395
 - Christian attitudes towards concept, 422–423
 - concept of, 20, 39–43
 - deep coma as mimicking, 116–117
 - defined, 7, 21, 110
 - irreversibility and, 26–28
 - maintenance of patient with, 208–209
 - neuropathology of, 29, 272–279
 - philosophical basis for, 419–420
 - protocols for decision-making in, 34
 - religious concepts of, 330–331
 - social ramifications of concept, 33–34
 - as symbol, 336, 337
 - term discussed, 28, 307–308
 - See also* Cerebral death; Criteria for brain death; Diagnosing brain death; Respirator brain
- Brain energetics, cerebral death and, 97–104
- Brain function, defined, 21
- Brain perfusion, ethics and, 396
- Brain scanning, 253
- Brain stem
 - in defectively perfused brains, 270
 - electrical activity in, 235
 - in respirator brain, 273
- Brain-stem auditory evoked responses, 127–128
- Brain-stem death
 - with cortical life, 129
 - defined, 7–8, 21
- Brain-stem function
 - absence of, 215–216
 - in comatose patients, 216
 - motor activity and, 217–218
- Brain-stem injury, simulation of brain death by, 116–117
- Brain weight, 279–280
- Bulbar reflexes in presumptive brain death, 79, 82
- Burst suppression, in EEG, 410

California Natural Death Act of 1976, 52, 54–58, 376

- chronology of, 388–390
- criticisms of, 380–381
- disobedience to, 391–392

- living will and, 380, 390–391
- opposition to, 379
- physicians' attitudes to, 382–383
- purpose of, 379
- rights of terminally ill under, 382
- California, 1974 statute in, 51, 354, 430
- Caloric response, *see* Vestibular reflex
- Caloric test on brain-dead patients, 253
- Capron-Kass model statute, 51, 349, 354, 361, 429–430
- Carbon monoxide poisoning, EEG in, 131
- Cardiac alterations in brain death, 252–256
- Cardiac arrest
 - apallic syndrome after, 210
 - cerebral ischemia secondary to, 88–89
 - EEG in, 282–290
 - effect on brain, 281
 - hypoxia from, 116
 - vegetative state and, 296
- Cardiac death, ECS and, 116
- Cardiovascular collapse, as criteria for brain death, 64
- Carotid angiography, 253
- Case law, on brain death, 426–428
- See also* Statutory definitions of death
- Catatonia, defined, 220
- Cathepsin, in postmortem autolysis, 276
- Central nervous system as control system, 25
- Cephalic reflexes
 - with cardiac arrest, 88
 - in CS study, 117–118
 - defined, 10, 113
 - and ECS, 73–74, 93, 114–116
 - frequency in normal persons, 87
 - in presumptive brain death, 71, 74–76, 90–93
 - with primary brain-stem lesions, 89
 - in respirator brain, 275–276
 - See also* specific reflexes
- Cerebellum
 - in brain death, 273, 283
 - in defectively perfused brains, 270
- Cerebral anoxia
 - in apallic syndrome, 201
 - survival after, 184–207
- Cerebral blood flow
 - angiography in demonstrating, 168–169, 231
 - in apallic syndrome, 184, 202, 204–205
 - bolus technique and, 143–163, 214, 231
 - cerebral circulatory deficit in, 180
 - in cerebral metabolism, 230–231
 - changes in status of, 208
 - in comatose patients, 158–160
 - computerized tomography and, 237

- Cerebral blood flow—(cont'd)
 direct demonstration of, 231–232
 echoencephalography in determining, 232–233
 EEG and, 129–130
 in establishing CMRO₂, 229
 experimental studies of, 98–104
 indirect demonstration of, 232–235
 inhalation techniques and, 232
 intracranial pressure and, 236
 measurements of, 97, 105
 pathology of brain death and, 279
 postmortem autolysis and, 277
 PvO₂ and, 229–230
 regional blood flow and, 106
 in sleep, 219
 tests for, 31, 143–144, 253
- Cerebral circulatory deficit, 180
- Cerebral death
 brain death vs., 95–96, 180, 356, 364–365, 367
 brain energetics and, 97–104
 concept of, 265, 267
 defined, 7, 10, 21
 legal issues in, 370–371
 metabolic criteria of, 228–230
 proposed statute on, 355–356
 techniques for confirmation of, 228–238
 term discussed, 200–201, 308
See also Brain death; Cognitive death; Neocortical death; Respirator brain
- Cerebral evoked response, equipment for, in ICUs, 400
- Cerebral metabolic rate of oxygen consumption (CMRO₂), 161, 228–229, 238
- Cerebral metabolism
 AVDO₂ in, 228–229
 cerebral blood flow in, 230–231
 CRMO₂ in, 228–229
 lactic acid in, 228–230
 PvO₂ in, 229–230
- Cerebral O₂ consumption, 253
- Cerebral oxidative metabolism, 105–107
- Cerebral temperature, in diagnosing brain death, 237
- Cerebral unresponsivity
 defined, 113
 ECS and, 114, 116, 130
- Cerebrospinal fluid, lactic acid content of, 230
- Cerebrum, role of, 265, 267
- Children, diagnosing brain death in, 163, 181–182
- Christianity
 * attitude towards death, 323, 329–337
 brain death concept and, 422–423
- Chronic vegetative states, *see* Persistent vegetative state
- Cognitive behavior, defined, 21
- Cognitive death
 law and, 339–341
 proposed statute on, 335–356
 “whole brain” approach vs., 356
See also Cerebral death
- Collaborative Study on Cerebral Survival, 419
 criteria for brain death in, 65
 methods of, 71–72
 results of, 72–94
- Coma
 alpha-frequency coma, 408, 409
 vs. apallic syndrome, 203
 apnea and, 216–217
 deep, 116–117, 158–159
 defined, 294
 differential diagnosis of, 215–218, 222–223
 as diminished state of consciousness, 219–220
 EEGs of patients in, 408–411
 evaluation of patients with long-standing, 412
 irreversible, 9
 nontraumatic, 296, 302
 oculovestibular responses in, 216–217
 patients with brain waves in, 117–119
 “pseudocomma,” 220–221
 pupillary fixation in, 216
 term discussed, 209
 theta-frequency coma, 408
 unresponsive, 8
See also Coma dépassé; Coma vigile; Deep coma; Nontraumatic coma; Reversible coma
- Coma dépassé, 7, 29, 70, 234
- Coma vigile, 184, 203
- Common law
 anatomical gift act and, 48–49
 definitions of death in, 48, 349, 350, 363
Commonwealth v. Golston, 351
- Computerized tomography, 237, 263, 277, 400–403
- Concept, defined, 6, 19–20
- Consciousness
 classification of states of, 218–223
 irreversible loss of, 314, 315
- Constructs, defined, 6, 19–20
- Consultants, problems related to, 412–413

Control systems, in living systems, 24-25
 Corneal reflex
 in apallic syndrome, 201
 with cardiac arrest, 88
 as criteria in brain death, 71, 73-75, 79, 82-87
 in presumed brain death, 80, 81, 92, 93
 in vegetative state, 298-300, 305
 Cortex, in respirator brain, 273-274
 Cortical life, with brain-stem death, 129
 Cost containment, 369, 374-375
 Cough reflex, as criteria for brain death, 71, 74, 75, 80, 85
 with cardiac arrest, 88
 in potential survivors, 93
 Criteria, defined, 6, 19-20
 Criteria for brain death, 20, 26, 138-139, 215-216, 412, 415
 cardiovascular collapse, 64
 current, 32
 development of, 28-31
 See also Electroencephalography; Harvard criteria
 Critical system, defined, 26-27
 CSF in diagnosing brain death, 238
 CT scan, *see* Computerized tomography

Death

brain-stem, 7-8, 21, 129
 Christian attitudes towards, 329-336
 concepts of, 20, 39-40, 308-313
 conceptual and technical questions in, 313-314
 criteria of, *see* Criteria of death
 determination of moment of, 329-330
 dual criteria of, 27-28
 Eastern attitude towards, 322-323
 as event, 22
 historical evolution of attitudes to, 11-17
 irreversible loss of consciousness as, 312-315
 loss of bodily integration as, 310-312, 314, 315
 loss of capacity for social interaction as, 312-314
 loss of the soul as, 309-310
 moral attitude towards, 322-327
 "natural," 335-336
 policy questions on, 315-317
 as process, 22
 statutory definitions of, *see* Statutory definitions of death
 systemic, 21
 terminology of, 20-22

Western attitude towards, 322-324
See also Brain death; Definition of death; Legal death
 Deceased, rights of, 41
 Declaration of Sydney, 30-31
 Deep coma
 CBF in, 158-159
 as mimicking brain death, 116-117
 Definition of death
 in Biblical law, 395
 in *Black's Law Dictionary*, 345, 425-426
 cerebral vs. brain death, 364-365
 classical, 23, 27
 common law, 349
 double vs. single standard, 354
 ethical issues in, 395-396
 legal, *see* Legal definition of death;
 Statutory definitions of death
 statutory, *see* Statutory definitions of death
 Delta waves in EEG, 408, 410, 411
 Depth recording of brain electrical activity, 234-235
 Diagnosing brain death, 413
 disconnecting tests in, 241-250
 etiologic basis for, 32
 pitfalls in, 216-223
 Diencephalon in brain death, 273
 Diminished consciousness, states of, 219
 Disconnecting tests, 241-250, 263
 Discrimination indices, 83-87
 Doll's-eye response, *see* Oculocephalic reflex
 Drug intoxication
 AVDO₂ in, 230
 deep coma and, 116
 in disconnecting test, 241
 ECS and, 122-123
 EEG in, 218
 as mimicking brain death, 32-33, 116-117
 as pitfall in diagnosis of brain death, 143, 216-218
 recovery from ECS and, 115-116
 in survivors of presumptive brain death, 76-83
 See also Barbiturate intoxication
 Dying, care of, 334-335
 See also Terminally ill patients
 Dynamic flow sequence, in bolus technique, 162

Echoencephalography, 232-233, 253
 Electrocardiogram (EKG), 122, 252-254

- Electrocerebral silence (ECS), 228, 408
 apnea and, 114, 116
 cardiac death and, 116
 cephalic reflexes and, 73, 93, 114-116
 clinical signs and, 128-129
 definition, 110-112
 drug intoxication and, 115-116, 122-126
 evoked potentials and, 127-128
 hypothermia and, 123-124, 211
 spinal reflexes and, 73-74, 115
 visual responses (VER) and, 127
- Electrocorticography, 112
- Electroencephalography, 112, 228, 262, 289
 in akinetic mutism, 203
 in apallic syndrome, 184, 202-203, 205
 blood pressure and, 233
 in brain death, 31, 110-119, 132, 253, 419
 in cardiac arrest, 282-290
 in coma dépassé, 29
 depth recording of, 234-235
 in diminished states of consciousness, 219-220
 evoked potentials in, 235
 ipsilateral changes in, 131
 isoelectric, 144
 in locked-in syndrome, 221
 misleading signs in, 130-131
 muscle artefact in, 406-408
 pitfalls in interpretation, 218, 281, 288
 prognostic value, 131-132, 284-285, 287-290
 reader concurrence, 112-113
 in respirator brain, 275-276
 steady potentials in, 235-236
 technical difficulties with, 121-122
 use in ICUs, 400, 403-410
 versus other criteria, 137-139
See also Electrocerebral silence
- Electromyogram (EMG), 122
- Electronystasmography test, 253
- Electro-oculogram (EOG), 122
- Electroretinogram (ERG), 122
- Entropy in open systems, 23-25
- Epicurean attitude towards death, 324
- Ethical issues
 in apallic syndrome, 206, 210
 in brain death, 41-43
 cerebral vs. brain death, 364-365, 367-368, 371
 in human experimentation, 318-319
 redefinition of death and, 337-338
 technology and, 325-328
- Euthanasia, 340
 arguments against, 372
 California Natural Death Act and, 380-382
 cerebral death and, 365
 as homicide, 368-369
 physician's role in, 369, 373-374
 statutory definitions of death and, 354
 termination of treatment and, 369-370
- Evoked cortical potentials, 235
 ECS and, 127-128
- Extracranial circulation in bolus technique, 157-159
- Eye movements
 in apallic syndrome, 304
 in vegetative state, 295, 297, 301-302, 304-305
See also Spontaneous eye movements
- F**uneral customs, history of, 11-13
- G**ag reflex, *see* Pharyngeal reflex
- Gamma imaging technique, 211-214, 253, 259
- Georgia, 1975 statute in, 51, 354, 430
- Glucose metabolism in brain, 106, 108
- Grave-robbing statutes, 46
- H**arvard criteria, 30, 41-42, 63, 66-67, 70, 308
 cerebral death and, 364-365
 common law conflict with, 48-49
 irreversible coma and, 311, 314
 legal issues and, 361-362
 validity of, 418-419
- Head trauma
 cerebral oxidative metabolism and, 105-107
 study of, in ICUs, 401
- "Heart" as metaphor, 331
- Herniation
 in brain, 267, 270
 effect on EEG, 130
- Homicide
 euthanasia as, 368-369
 termination of treatment as, 340-342, 345-346
- Hospitals, terminally ill in, 327
- Human experimentation
 ethical issues in, 41-42, 318-319
 legal guidelines in, 359-361

- Hypercapnic acidosis, in disconnecting tests, 245
- Hypersomnia, 219-220, 222
- Hyperventilation, in disconnecting tests, 241
- Hypotension, in presumptive brain death, 76
- Hypothermia, 72-73
 - ECS with, 123-124, 211
 - spontaneous, apnea and, 241

- I**daho, 1977 statute in, 51, 354, 430
- Induced movements
 - correlation with ECS, 74, 115
 - as criteria in brain death, 71-72, 75, 84-86, 92
 - in survivors, 80
- Infants, diagnosing brain death in, 163, 181-182
- Information
 - definition of, 24
 - in open systems, 24-26
- Informed consent, patients', 378
- Inhalation techniques, in demonstrating CBF, 232
- Intensive care units, 33
 - baseline studies by, 401
 - equipment in, 400
 - neurophysiology laboratories in, 398
 - personnel in, 400
- Intra-arterial isotope perfusion in demonstrating CBF, 232
- Intracerebral techniques of demonstrating CBF, 232
- Intracranial angiography
 - cerebral infarction and, 169
 - circulation in posterior fossa, 174, 178, 180-181
 - extravasation in, 174, 178-179, 181
 - intracranial hemorrhage and, 169
 - transtentorial hippocampal herniation, 174
 - See also* Angiography
- Intracranial blood flow, 157, 169, 172-175, 180-181
 - brain destruction and, 418
 - See also* Cerebral blood flow
- Intracranial pressure in diagnosing brain death, 236, 238, 253, 261
- Intrathecal injection of radioiodinated serum albumin, 253
- Intrathecal spinal injection of RISA, to determine brain death, 236
- Iowa, 1974 statute in, 430

- Irreversible coma
 - brain death vs., 28, 222
 - defined, 9, 21
 - in Harvard criteria, 311, 314
 - See also* Apallic syndrome; Irreversible noncognitive state; Neocortical death; Persistent vegetative state
- Irreversible noncognitive state, 21
- Ischemia
 - EEG in, 284, 286-287, 289
 - resistance to, 130
- Isoelectric EEG
 - in comatose patients, 217
 - conditions producing, 234
 - See also* Electroencephalogram
- Isotope angiography, 231, 238, 259-262

- J**apanese criteria of brain death, 64, 66-67
- Jaw jerk
 - with cardiac arrest, 88
 - as criteria of brain death, 71, 73-75, 79-82, 85, 91
 - in normal subjects, 87
- Jewish law, accord of brain death concept with, 420-422
 - See also* Biblical law

- K**ansas, 1970 statute in, 344, 354, 428-429
- Knee reflexes as criteria in brain death, 71, 84-86

- L**actic acid
 - in cerebral metabolism, 228-231
 - as content of cerebrospinal fluid, 230
 - in postmortem autolysis, 277
- Legal definition of death, 48-52
 - effect on administration of justice, 350
 - interests of society in, 49
 - judicial role in framing, 351
 - legislative role in framing, 352
 - medical expertise and, 49, 350-351
 - uncertainty about, 350
- Legal fictions, 349
- Legislation
 - on organ transplantation, 45-49, 423-425
 - on termination of treatment, 52-58, 342
 - See also* Statutory definitions of death

Life

- definition of, 22-23
- potential for, 23
- sacredness of, 331-334
- See also* Living systems

Light reflex, *see* Pupillary reflex

Living systems

- control systems of, 24-25
- irreversible states of, 26-28
- as open systems, 23-24
- See also* Open systems

"Living will" laws, 343

- California Natural Death Act and, 380, 390-391

Locked-in syndrome, 203, 220-221

- differential diagnosis of, 225-226

Mari case, 52

Maryland, 1972 statute in, 349, 429

Medical research and attitudes towards death, 324-325

Medical technology, needs of terminally ill and, 377

Medicine, cultic qualities of, 325-326

Meprobamate intoxication, ECS and, 122

Mercy killing, euthanasia distinguished from, 381-382

- See also* Euthanasia

Metabolic changes in brain death, 252, 255

Metabolism, cerebral, *see* Cerebral metabolism

Michigan, 1975 statute in, 430

Midbrain reticular formation lesions, 106

Montana, 1977 statute in, 430

Moral issues, *see* Ethical issues

Motor abnormalities in coma, 219-220

Motor activity

- in comatose patients, 217
- drug intoxication and, 218
- in presumptive brain death, 74-76
- in vegetative state, 294, 295, 298-299, 300, 302

Movements, correlation with ECS, 115

- See also* Induced movements; Spontaneous movements

Muscle tone

- with cardiac arrest, 88
- as criteria in brain death, 71, 78, 85-86, 92

Myoclonic jerks, in EEG, 410

"Natural death", 335-336

Negentropy, 25

Neocortical death

- Christian view of, 333-334

defined, 8

- as irreversible coma, 21

- term debated, 200-201

- See also* Cerebral death

Nervous system, plasticity in, 107

Neurologic recovery, from coma, 294-296

Neurons, in patients with absent bolus, 267

Neurophysiology laboratories, in ICUs, 398, 399

Neuroscience progress sheets, in ICUs, 401

New Hampshire, 1977 right-to-die law, 52

New Mexico, 1973 statute in, 52, 429

New York City Health & Hospitals v. Sulsona, 50

New York State Anatomical Gifts Act, 428

NINDS Collaborative Study, 63

Noncognitive states

- brain death vs., 28

- defined, 8-9

Nontraumatic coma, 296, 302

North Carolina, 1977 statute in, 52, 357

Nurses in ICUs, 400

Ocular reflexes in presumptive brain death, 79, 82

Oculocephalic reflex

- cardiac arrest with, 88

- as criteria in brain death, 71, 74, 75, 83-87

- depth of unconsciousness and, 209

- in presumed brain death, 91-93

- in vegetative state, 298

Oculovestibular response

- in comatose patients, 216-217

- as criteria for brain death, 215-216

- depth of unconsciousness and, 209

- in vegetative state, 298

Oklahoma, 1975 statute, 51, 430-431

Open systems

- defined, 21-22

- information in, 24-26

- See also* Living systems

Ophthalmic artery blood flow in determining CBF, 233-234

- Organ transplantation, 30-31
 - anencephalic donors, 141-142
 - apallic syndrome and, 210
 - ethical issues in, 41-42, 396-397
 - "extraordinary care" and, 33
 - hypotension and, 64
 - legal barriers to, 45-50
 - problems of supply, 47
 - role of ICUs in, 411-412
 - statutes on, 45-49, 423-425
 - See also* Uniform Anatomical Gift Act
- Orthodox Jewish law, *see* Jewish law
- Oregon, 1975 statute in, 51, 429
- Oxidative metabolism
 - of brain, 97-98
 - experimental study, 98-103
- Oxygen uptake in disconnecting tests, 246

P

ancurionium bromide in determining ECS, 408

- Parental decisions in termination of treatment, 344-345
- Pathology of brain death, 272-279
- Patient consent, experimentation and, 360
- Patients' rights, 41
 - termination of treatment and, 53-56, 328, 341, 378-379, 382

People v. Flores, 351

People v. Lyons, 370-371, 427

Perioral facial reflex, *see* Snout reflex

- Persistent vegetative state
 - defined, 8-9, 219-222
 - neocortical death and, 8, 21, 27, 160
 - proposed statute on, 355-356
 - term discussed, 224-225

See also Quinlan case

Pharyngeal reflex

- cardiac arrest with, 88
- as criteria for brain death, 71, 74, 75, 80, 83, 85
- in survivors, 80, 93

Physicians

- California Natural Death Act and, 382-383, 391-393
- euthanasia, 369, 373-374
- needs of terminally ill and, 377
- social attitudes towards, 323-326
- statutory definition of death and, 424-425
- termination of treatment and, 341-342, 344, 345

Pius XII, proclamation of, 28-29

Plantar responses as criteria in brain death, 71, 84, 85, 91-92

Posterior fossa

- circulation in, 174, 178, 180-181
- EEG and lesions in, 130
- exclusion of, in bolus technique, 145
- in respirator brain, 276-277
- Postmortem autolysis, biochemical changes in, 276-277
- Primary diagnoses, correlation with EEG, 113, 114
- Privacy, right to, 378
- "Prolongation of Life, The" (Pius XII), 28-29
- Protestant thought, accord of brain death concept with, 423
- "Pseudocoma," 220-222
- "Pseudo-isoelectric" EEG, 122-123
- Psychological problems, related to coma, 413

Pulmonary insufficiency, disconnecting test with, 263

Pupillary fixation, in comatose patients, 216-217

Pupillary reflex

- in apallic syndrome, 201
- in cardiac arrest, 88
- in coma, 219-220
- as criteria in brain death, 71, 74, 75, 82-87
- in presumed brain death, 91-93

Pupil size

- with cardiac arrest, 88, 93
- in presumed brain death, 90-91, 93, 215

PVO₂, in determining brain death, 238

PVS, apallic syndrome and, 9

Quinlan case, 52, 320-321, 334-341, 425

termination of treatment and, 346-347

R

adial reflexes as criteria of brain death, 71, 85

Radioactive tracers

- in evaluating cerebral circulation, 143-163

¹³³Xe isotope technique, 185, 203, 205

See also Bolus technique

Radioisotopic bolus technique, 31, 130

medical ethics and, 395

See also Bolus technique

Regina v. Potter, 351

Regional brain glucose metabolism, 106

- Religious attitudes
 history of, towards death, 11-14
 toward identification of person with
 brain death, 42-43
- REM sleep, 218-219
- Research, *see* Human experimentation
- Respiration
 in coma, 219
 in survivors, 77, 78, 80
See also Spontaneous respiration
- Respirator brain, 9, 87, 89, 275-278
- Respiratory pattern in vegetative state,
 298
- Resuscitation
 after cardiac arrest, 281, 284-290
 quality of survival after, 283, 287-288
 stages after, 287-289
- Reticular formation lesions, 105-107
- Reye's syndrome, 410
- Rheoencephalography, 234, 238
- RISA, spinal injection of, to determine
 brain death, 236
- Roman Catholic ethics, accord of brain
 death concept with, 422-423
- Rostral reorganization, 107, 108
- Rostral reticular formation lesions, 106
- S**
 Scavenger cells, in patients with defec-
 tively perfused brains, 270
- Seizures, treatment of, 410-411
- Simultaneous bilateral reticular formation
 lesions, 106
- Skeletal muscle tone, in vegetative state,
 295, 299
- Sleep, 218-219
- Slow-wave sleep, 218-219
- "Small" bolus, 214
- Smith v. Smith*, 426
- Snout reflex
 cardiac arrest with, 88
 as criteria of brain death, 71, 73-75,
 79-80, 82-83, 85, 91
 in normal subjects, 87
- Social interaction, loss of capacity for
 as definition of death, 312, 314
- Soul, loss of, as definition of death, 309-
 310
- Spinal cord
 with absence of bolus, 267
 in respirator brain, 272-273
- Spinal reflexes, 10, 85, 86, 418-419
 in apallic syndrome, 201
 defined, 10
 as discrimination indices, 74-76, 84, 91,
 218
 ECS and, 73-74, 115
 in locked-in syndrome, 225-227
 in survivors, 81-83
- Spindle activity, in EEG, 408, 410, 411
- Spontaneous eye movements, in vegetative
 state, 295, 298
- Spontaneous hypothermia, apnea and, 241
- Spontaneous movement
 with cardiac arrest, 88
 as criteria in brain death, 71-72, 75,
 84-87, 92
 with ECS, 74, 115
- Spontaneous respiration
 in biblical sources, 421
 in comatose patients, 217
 in presumptive brain death, 83, 84,
 215-216
 testing for, 413
- State v. Brown*, 426
- Statutory "conscience clause," 356-357
- Statutory definitions of death, 50-52, 363
 American Bar Association (1975), 51,
 356, 365-366
 California (1974), 354
 Capron-Kass model statute (1972), 51,
 349, 354, 361
 degree of specificity in, 352
 euthanasia and, 354
 Georgia (1976), 51, 354
 Idaho (1977), 354
 Kansas (1970), 50, 51, 349, 353, 354
 Maryland (1972), 349
 medical opposition to, 350, 353
 North Carolina (1977), 357
 Oklahoma, 51
 Oregon (1975), 51
 scientific basis for, 353
 uniformity in, 352-353, 357
See also Case law
- Steady potentials, in diagnosing brain
 death, 235-236
- Stroke, ICUs and, 401, 403, 404
- Subcortical activity, ECS and, 126-127
- Succinylcholine, 406-408
- Suicide
 euthanasia as, 369
 rejection of treatment and, 370
- Suppression burst pattern, in EEG, 123
- Survival, quality of, 287-289
- Survivors, of presumptive brain death,
 76-83
- Swallow reflex
 as criteria of brain death, 71, 74, 75,
 84, 85
 in survivors of presumptive brain death,
 80, 81, 93
- Swedish criteria of brain death, 64, 66-67
- Systemic death, defined, 6, 21

- T**chnetium pertechnetate, in bolus technique, 145
- Technetium sulfur colloid, in bolus technique, 145
- Technology, moral issues and, 325-328
- Tendon reflexes
in presumed brain death, 91
in vegetative state, 295, 299
- Tennessee, 1976 statute in, 431
- Terminally ill patients
medical technology and, 377
preparation of health professionals and, 377
and specialization of medicine, 377
See also Dying
- Termination of treatment
changes in physician's role, 341-342
distinguished from euthanasia, 369-370
legislation and, 52-58, 342, 344-348
nonlegislative options, 343-344
patient's choice of, 328
Quinlan case and, 339-340
- Thalamic system in apallic syndrome, 210-211
- Thalamus
electrical activity of, 235
rostral reorganization at level of, 107
- Theta coma, 407-409, 412
- Thermodynamics, open systems and, 23-24
- Thomas v. Anderson*, 426
- Total brain infarction, *see* Brain death
- Transitory ischemia, *see* Ischemia
- Transplantation, *see* Organ transplantation
- Transtentorial hippocampal herniation, 174
- Triceps reflex as criteria of brain death, 71, 85
- Triphasic waves, in EEG, 131
- Tucker v. Lower*, 351, 371, 426-427
- "Twilight states," in California Natural Death Act, 380
- U**ncontrolled seizures, treatment of, 410-411
- Uniform Anatomical Gift Act, 46-50, 316, 430
- Unresponsive coma, defined, 8
- V**alue theory, 25-26
- Vascular endothelium in defectively perfused brains, 270
- Vascular filling in brain death, 161
- Vegetative behavior, defined, 21
- Vegetative state
defined, 294
early prediction of, 299-300
nontraumatic causes of, 296
prognosis, 293-303
See also Persistent vegetative state
- Verbal responses in vegetative state, 295, 297
- Vertebral angiography, 253
- Vestibular reflex
cardiac arrest with, 88
as criteria in brain death, 71, 74, 75, 79, 82-87
in presumed brain death, 91, 92, 93
- Vestibulo-ocular reflex in coma, 219
- Virginia, 1973 statute in, 429
- Visual responses (VER) in patients with ECS, 127
- "Vital" body fluids and definition of death, 310
- Vital signs, predictive value of, 113-114
- W**akefulness, 218-219, 293
- West Virginia, 1975 statute in, 430
- ¹³³**X**e isotope technique, 185, 203, 205



Author Index

(Italicized page numbers refer to comments in discussions)

Abkowitz, M. A., 459-466

Akhtar, M., 726-736

Allen, W. N., 759-766

Amiell, J., 467-480

Andersen, Jan R., 293-300, 343-354

Anzai, Hiroyuki, 256-268

Ashwell, G. J., 417-441

Balch, Alan L., 651-662

Barton, Jacqueline K., 686-700

Baughman, R. H., 705-725, 775-787

Bechgaard, Klaus, 293-300, 467-480

Bloch, Aaron N., 165, 209, 332, 366-368, 458

Bradley, Mark G., 588-593

Bray, J. W., 407-416

Brill, J. W., 459-466

Burlich, James, 799

Candela, G. A., 377-381

Cape, T., 377-381

Cava, M. P., 355-360

Chaikin, Paul M., 128-144, 459-466

Chance, R. R., 705-725

Chartier, Duane, 788-799

Chen, C. H., 78

Chiang, C. K., 726-736

Clardy, J., 382-394

Clark, R. J. H., 495, 672-685

Cohen, M. J., 726-736

Coleman, Lawrence B., 316-332, 441, 458

Coler, M., 538

Comès, Robert, 234-243, 406

Conwell, Esther, 183-209, 458

Coppens, P., 60, 244-255, 538

Cornish, T. F., 525-538

Cowan, Dwaine O., 366-368

Craven, Robert A., 343-354

Cuellar, E., 580-587

Cutforth, Brent D., 788-799

Datars, W. Ross, 788-799

Dauplaise, D., 382-394

Davis, M., 744

Day, P., 9-24, 110, 495, 558

DeCorpo, J. J., 759-766

Delhaes, P., 467-480

Duke, C. B., 166-178, 315, 331

Elbaum, C., 745-758

Eley, D. D., 417-441

El Sharif, Mohammed, 663-671

Endres, Helmut, 617-632, 663-671

Engler, Edward M., 60, 78, 293-300, 343-354

Epstein, Arthur J., 165, 183-209, 233, 416, 458, 459-466

Etemad, Shahab, 343-354, 737-744

Fabre, J. M., 467-480

Ferguson, Richard, 822

Finnegan, T. F., 377-381

Fitcher, D. B., 771-774

Flandrois, S., 467-480

Froix, M. F., 459-466

Gamble, F. R., 86-110

Garito, A. F., 301-315

Geiss, R. H., 737-744

Geoffroy, Gregory L., 588-593

Gill, W. D., 737-744, 771-774

Gillespie, Ronald J., 788-799

Giral, L., 467-480

Glick, M., 377-381

Gliemann, Günter, 539-559

Goetz, Fred, 360, 736

Gordon, J. G., II, 580-587, 593

Grant, Paul, 291

Gray, H. B., 580-587

Green, Dennis C., 361-365

Greene, R. L., 737-744

Griffiths, C. H., 459-466

Gunning, W., 459-466

Hadek, V., 580-587

Haen, P., 701-704

Hart, H. R., Jr., 407-416

Hashmall, J. A., 377-381

Heeger, A. J., 331, 332, 459-466, 726-736, 800-822

Hoffman, Brian, 538, 616

Hsu, C.-H., 580-587

Ilsley, W., 377-381

Interrante, L. V., 407-416, 616

Iqbal, Z., 775-787

Isett, L. C., 61-78, 395-406, 416

Jacobsen, C. S., 467-480

Johnson, P. L., 525-538

Junker, W. R., 745-758

Kao, H. I., 745-758

Kasper, J. S., 407-416
 Keeney, Mark E., 588-593
 Kelber, J., 525-538
 Keller Heimo J., 442-458, 617-632, 662, 663-671
 Keryer, G., 467-480
 Kistenmacher, Thomas J., 333-342, 538
 Klemm, Richard A., 144
 Kleppinger, J., 726-736, 775-787
 Kokoszka, G. F., 377-381
 Kommandeur, J., 315, 725
 Krug, William P., 366-368
 Kruger, A. A., 79-85
 Kutner, Włodzimers, 767-770
 Kuyper, J., 737-744

Labes, M. M., 745-758
 Lakshmikantham, M. V., 355-360
 LaPlaca, S. J., 369-376
 Lehmann, R., 617-632
 Lippard, Stephen J., 686-700
 Little, W. A., 459-466
 Louis, E. J., 726-736
 Love, P., 745-758

MacDiarmid, Alan G., 726-736, 757, 767-770, 775-787, 799, 800-822
 Mah, P. T., 759-766
 Mann, K., 580-587
 Mark, Harry B., Jr., 767-770
 Marks, Tobin J., 594-616, 822
 Martin, Reinhold, 663-671
 McGhie, A. R., 301-315
 Meerschaut, A., 701-704
 Mègnamisi-Bélombé, Michel, 633-650
 Megtert, S., 234-243
 Meinwald, J., 382-394
 Metzger, Robert Melville, 145-165, 255, 292
 Meyer, Thomas J., 496-508
 Miller, Joel S., 1-8, 25-60, 183-209, 459-466, 616
 Milliken, J., 726-736
 Monceau, P., 701-704
 Moran, M. J., 726-736
 Morawitz, H., 179-182
 Moroni, W., 442-458
 Murakami, Mutsuaki, 269-292
 Myer, G., 745-758

Nigrey, P. J., 301-315
 Nöthe, D., 442-458
 Novatny, M., 459-466
 Nowak, Robert, 767-770

Ohno, Teruaki, 256-268
 Ong, N. P., 292

Pasquali, G., 525-538
 Patel, Vishnu V., 343-354
 Peebles, D. L., 726-736
 Perez-Albuerné, E. A., 395-406
 Perlstein, J. H., 61-78, 209, 291, 457, 616
 Peterson, Selmer W., 560-579
 Piacente, P. A., 407-416
 Poehler, Theodore O., 366-368
 Pouget, J. P., 234-243
 Poveda, Arnulfo, 617-632
 Putnik, C., 525-538

Reis, Arthur H., 110, 560-579
 Reynolds, G. A., 61-78
 Rouxel, Jean, 110, 701-704
 Row, T. N. Guru, 244-255

Saalfeld, F. E., 759-766
 Salamon, M. B., 525-538
 Samson, S., 580-587
 Saran, Mohan, 744
 Schaffman, M. J., 525-538
 Schechtman, Barry, 725
 Schultz, A. J., 509-515, 525-538
 Scott, Bruce A., 343-354, 369-376
 Scott, J. C., 382-394
 Shirakawa, H., 726-736
 Siedle, A. R., 232, 360, 377-381, 766
 Silverman, B. D., 165, 369-376
 Slade, M. L., 459-466
 Smith, R. D., 737-744
 Somoano, R., 110, 292, 441, 580-587
 Soos, Z. G., 127, 442-458, 725
 Stanley, George C., 593
 Street, G. B., 737-744, 771-774
 Stucky, Galen, 525-538

Takabe, Teruhiro, 256-268
 Tanaka, Chizuko, 256-268
 Tanaka, Jiro, 256-268
 Tanaka, Masashi, 256-268
 Tanner, D. B., 459-466
 Taube, Henry, 481-495
 Temkin, H., 382-394, 771-774
 Thomas, G. A., 79-85
 Träger, Ulrich, 663-671
 Tomkiewicz, Yaffa, 343-354
 Torailles, E., 467-480
 Torrance, J., 24, 210-233, 369-376, 538, 559

Underhill, A. E., 516-524

Van Allen, J. A., 61-78
 Van de Sand, H., 617-632

Van Duyne, R. P., 377-381
Van Schyndel, André, 788-799
Vu, Dong, 617-632

Wallwork, S. C., 417-441
Washecheck, D. M., 525-538
Watkins, G. D., 407-416
Welber, B., 369-376
Willett, Roger D., 111-127
Williams, Jack M., 509-515, 525-538
Williams, R., 580-587

Willis, M. R., 417-441
Wood, D. J., 516-524
Woodward, J., 417-441
Woyciesjes, P. M., 377-381
Wudl, F., 79-85, 360, 736
Wyatt, J. R., 759-766

Yamagishi, F. G., 301-315
Yersin, Hartmut, 539-559
Yoshimura, Susumu, 269-292

